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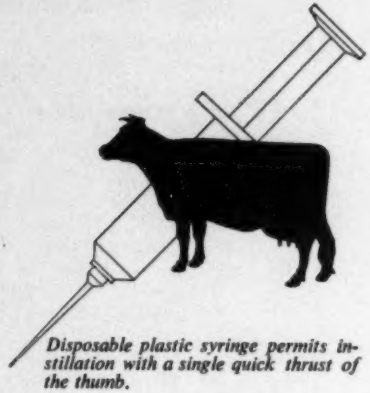

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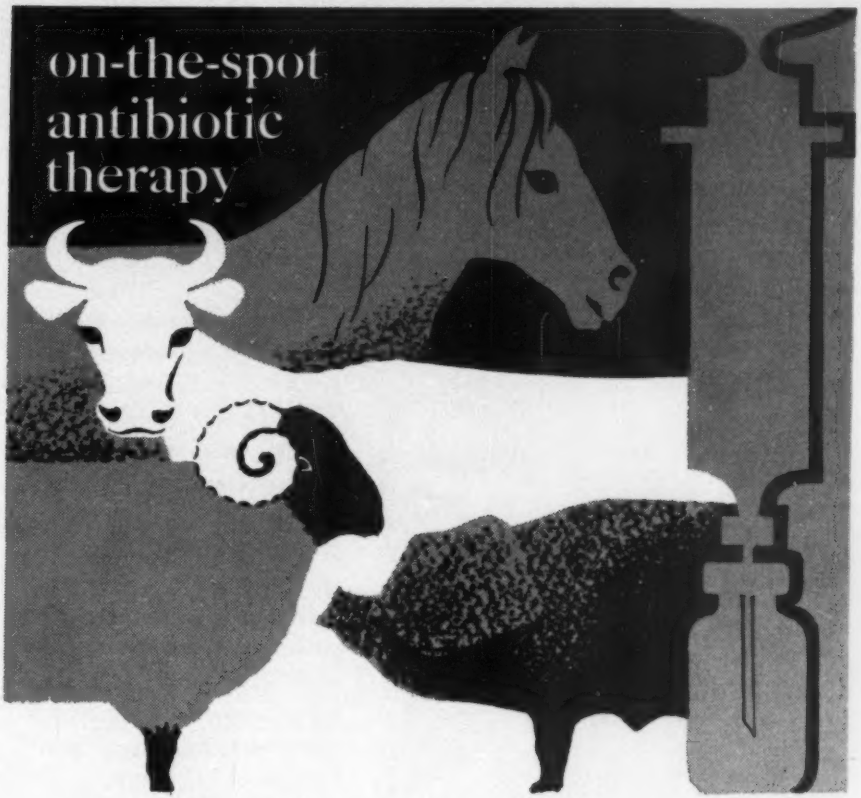

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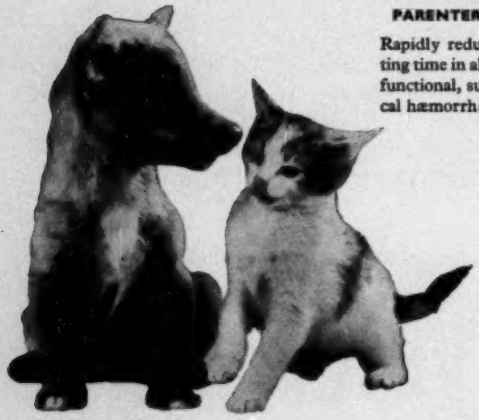

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THE WORLD VETERINARY POULTRY ASSOCIATION CONGRESS AT UTRECHT

There has been a tendency to belittle the efforts of the veterinary profession in the control of avian diseases. Although this may be true as far as direct contact between the veterinary practitioner and the poultry farmer is concerned, it is equally true that the poultry industry could not have expanded as it has done, to become one of the major branches of agriculture in most countries, without the efforts of the relatively few avian pathologists, diagnosticians and veterinary field officers. The successful formation of the World Veterinary Poultry Association as an affiliated specialist branch of the World Veterinary Association is a gratifying indication of our profession's increasing interest in this highly important field of food production.

The formation of an international association of poultry pathologists, first initiated by Professor de Blieck and Dr. R. F. Gordon in 1955, was formally adopted at the XVIth World Veterinary Congress in Madrid in 1959. The Association now has a membership of some 800 veterinarians in 24 countries, whilst national associations have been established in the U.S.A., Great Britain, Netherlands, France, Western Germany and Japan, and others are in the process of formation. The British Veterinary Poultry Association has a membership of over 80.

An historical survey of the formation of the World Veterinary Poultry Association, its aims and objects, was given by Professor de Blieck in his presidential address at the opening of the Association's first Conference, which was held in Utrecht in November 1960 when approximately 150 members attended from 20 different countries. The unexpected response to this Conference taxed to the limit the resources of the new Association and the Conference could not have taken place without the generous financial assistance which was given by commercial organizations in the United Kingdom.

At the closing session of the Conference, Dr. W. P. Blount presented to Professor de Blieck, on behalf of the British Veterinary Poultry Association, a presidential chain of office in Dutch silver, and as a further tribute to his work in stimulating the formation of the Association Professor de Blieck was elected an Honorary Life President. The other office-bearers elected were *President:* Prof. A. Brion (France); *Vice Presidents:* Prof. P. P. Levine (U.S.A.) and Dr. R. F. Gordon (G.B.); *Secretary/Treasurer:* Dr. W. M. McKay (G.B.); *Assistant Secretary:* Prof. Fritzsche (West Germany).

This number of the *British Veterinary Journal* has been placed at the Association's disposal for the publication of the papers presented at its first Conference. Unfortunately lack of space precludes the publication of the full proceedings

here. Only the six main papers by leading workers in their particular fields and dealing with three of the major problems of the poultry industry, namely Newcastle disease, chronic respiratory complex and the leucosis complex, are included. The five following shorter communications will appear in subsequent issues of the Journal this year:

Haemorrhagic syndrome, Dr. Marthedal.
Duck plague, Professor Jansen.
Avian encephalogyelitis, Dr. Guillon.
Prophylactic effect of vitamin A on caecal coccidiosis, Dr. Gerriets.
Hygiene of poultry husbandry and feeding, Dr. Siegmann.

Brit. vet. J. (1961), 117, 275

THE CONTROL OF NEWCASTLE DISEASE IN GREAT BRITAIN

By John Reid

Animal Health Division, Ministry of Agriculture, Fisheries and Food, London

The first recorded outbreak of Newcastle disease in Great Britain was the one in which Doyle made his classical investigation in 1926 when he isolated the causal virus in a flock near Newcastle-on-Tyne. The origin was attributed to the feeding of poultry on infected offal from a ship in the nearby port. The infection was of a very virulent type and all the birds in the flock died. In the following year an apparently similar disease occurred in a few counties in the south of England; the mortality was again very high. Only a few flocks were affected and the infection apparently died out.

The disease did not appear again until 1933 when it struck a large flock in Hertfordshire. The mortality was very high and the owner slaughtered the survivors and carried out a thorough disinfection of the premises. The disease apparently did not spread to any other flocks. Investigation of the outbreak did not disclose the origin of the infection.

Fowl Pest Order

In 1935 the powers in the Diseases of Animals Act for the control and eradication of disease were extended to include diseases of poultry, and in 1936 the Fowl Pest Order was introduced. "Fowl pest" in this legal context includes by definition two diseases—Newcastle disease and fowl plague. While fowl plague may possibly have been in Great Britain at an earlier date it has not been recorded since 1922. Therefore all the outbreaks dealt with under the Order are of Newcastle disease. This Order requires owners or persons in charge of poultry to notify suspicions of the existence of the disease to the police. It lays the same onus on a veterinary surgeon who may suspect the disease in the course of his private practice. It empowers the Minister of Agriculture to slaughter affected poultry and poultry exposed to the infection and to pay compensation for fowls not affected at the time of slaughter. It provides for the premises where the disease exists to be declared an Infected Place and specifies rules which must be applied to restrict the movement of poultry, manure and equipment, in order to prevent the spread of infection. The Order also makes provision for the cleansing and disinfection of the premises and of vehicles and utensils which may have been contaminated with virus. The general enforcement of the Order is the responsibility of the local authorities. A local authority is the Council of a county or of a large town. It has important duties of a non-veterinary character under the Diseases of Animals Act, including the promulgation of the Ministry of Agriculture's orders, the appointment of inspectors to enforce the orders, the issue, when necessary, of special authority for the holding of livestock markets and the

issue of licences. There are 344 local authorities in Great Britain and almost invariably their enforcement duties are carried out by the police. The closest co-operation between local authorities, the police and the Ministry's officers is essential.

NEWCASTLE DISEASE IN GREAT BRITAIN, 1947-1950

Epizootiology

In February 1947 Newcastle disease appeared in England for the third time. At this time the importation of poultry carcases from Europe had begun to help to meet the continuing food scarcity. The outbreak occurred two weeks after the first importation of these carcases. Some of the supplying countries, notably Hungary and Poland, had sustained severe epidemics of the disease which had spread from the Far East during the war years to such an extent that it was present in most European countries at the end of the war. The symptoms in infected flocks were peracute in character and mortality was very high. In a majority of *primary* cases it was noted that the affected fowls had been fed on untreated waste foods containing poultry offal and trimmings. A case is accepted as being primary if no connection can be discovered between it and another existing case. Of the first 542 cases, 72 per cent of the fowls belonged to domestic poultry-keepers—householders who kept a few birds to provide eggs for the family. The origin of infection was attributed as follows:

in 42% of cases to the purchase of replacement fowls from dealers, markets and pet shops;
in 33% to unboiled swill and poultry offal;
in 8% to contact with neighbouring infected flocks;
in 7% to indirect contact with infected clothing and equipment; and
in 10% no origin could be discovered.

At this particular time animal feeding stuffs were still in short supply and distributed under a rationing system. In an effort to conserve feeding stuffs large amounts of waste food from canteens, hotels and other catering establishments were utilized to feed poultry and pigs during the war and early post-war years. Once established, the disease was spread mainly by the movement of live birds during the incubation stage, generally through the agency of dealers or auction markets.

Random samples of tissues—mainly portions of skin from imported carcases—were tested at the Ministry's Central Laboratory at Weybridge by the inoculation of fowls and egg embryos, and a high proportion of consignments comprising frozen carcases of domestic fowls, turkeys, ducks and geese, were found to be infected. An analysis of the results showed:

young fowls	69%	infected
hens	66%	,,
old cocks	80%	,,
geese	6·9%	,,
ducks	11%	,,
turkeys	24%	,,

Procedure

It was decided to adopt a stamping-out policy including the essential measures to control the movement of poultry. It was obviously necessary to take certain ancillary steps including the stoppage of import of infective material and the prohibition of the feeding of uncooked garbage to poultry.

Importation of Poultry and Hatching Eggs Order. Consequently the Importation of Poultry and Hatching Eggs Order, 1947, was introduced to prohibit the landing of live poultry or hatching eggs from specified countries where Newcastle disease was known to exist.

Boiling of Waste Foods Order. The Boiling of Waste Foods Order, which had for many years been the first-line defence against foot-and-mouth disease and swine fever, was extended to include poultry and it became an offence to feed to poultry or to allow them to have access to waste food that had not been boiled for one hour. For reasons of shortage of food and on political grounds it was not possible to prohibit the importation of poultry carcases, but arrangements were made for them to be eviscerated in the country of origin. The movement of live poultry into Scotland and the north of England from the rest of England and Wales was prohibited.

With these legislative measures, along with prompt reporting of disease, the field veterinary staff, already widely deployed throughout the country to deal with animal disease generally, were able to deal competently and quickly with diagnosis and disposal of infected birds. Veterinary officers quickly gained experience of the history, symptoms and typical post-mortem lesions associated with the disease.

In 1947, 2,222 outbreaks were confirmed in 45 counties in England and Wales. The heaviest infection was in small flocks around the large towns in the industrial Midlands of England and in the eastern counties. In the following year, there was a marked reduction in the number of outbreaks; only 267 were confirmed and these were for the most part limited to the Midlands and to the south-east of England. In 1948 a "low" form of the disease appeared in the rearing station attached to a large hatchery; this was disclosed after the discovery that fowls from this station which had been sent to a laying trial were positive to the haemagglutination inhibition test. If this type of infection had been widespread in the country it would have reduced the value of the test for confirmatory purposes. A survey of similar flocks and establishments was therefore made with negative results, which gave some assurance that this infection of a sub-clinical nature was not widely spread. In the early part of 1949 there was a continued decline in outbreaks, followed later by a widespread series of primary cases in which again the great weight of infection appeared in flocks belonging to domestic poultry-keepers.

Zoning of imported carcases. Importation of carcases from Europe continued and in addition sampling by biological tests was continued so that especially dangerous consignments could be directed for consumption to places where, if infection escaped, it was likely to have the least harmful effect on the national poultry industry. This system of zoning, arranged by the Ministry of Food, who were then the only importers, ensured that the carcases could be directed

to five large industrial areas. Senior veterinary officers visited Europe to see what steps could be taken to prevent infected carcases being sent to Great Britain. There is no doubt that on some of the killing plants the collection of poultry did allow a build-up of infection in birds awaiting slaughter, with the consequence that poultry of all categories were killed when they were in the incubation stage. The great need to import food at the time did not allow the importation of carcases to be stopped, but it was possible to get the exporting countries to take steps to reduce infection within their slaughtering places.

Newcastle disease in Scotland

A new feature in 1949 was the confirmation of Newcastle disease in Scotland which up till then had been kept clean by a ban on the movement of all live poultry from England and Wales. Disease was first confirmed in two flocks in the Orkney Islands and investigations very soon revealed others and a disclosure that there had been Newcastle disease in the vicinity for several weeks. The disease spread quickly along the north-west coast to the Inner and Outer Hebrides. There was comparatively little movement of live birds and there were very few auction markets in the areas involved. Outbreaks spread to the east of Scotland and again were limited to coastal districts; they were recorded in an inland loch in Aberdeenshire and as far south as the Bass Rock in the Firth of Forth.

Role of sea-birds in the transmission of Newcastle disease. Special investigations were undertaken by the veterinary staff and although exhaustive enquiries failed to reveal conclusively the source of the original infection, the coastal distribution suggested that sea-birds might be incriminated. Efforts were made to obtain specimens of sea-birds and in the subsequent laboratory work, in which the haemagglutination inhibition test and virus recovery were used, shags, cormorants and gannets were found to be infected. It was therefore tentatively concluded that infection was introduced by swill containing poultry offal from passing ships. It became known also that a large number of carcases of poultry affected with the disease had been thrown into the sea. Fowl typhoid had been troublesome in the islands to the north-west of Scotland for many years and the symptoms of that disease could be confused with peracute Newcastle disease; for this reason there was delay in reporting. It seems fairly certain that sea-birds became infected and played a part in spreading disease around the coast. Further, the only recorded cases in Northern Ireland were confirmed a few weeks after this Scottish series and the first outbreak was discovered in a small farm near the sea a little over forty miles from the Scottish coast where outbreaks had recently occurred.

Although disease continued to occur in Scotland for nearly a year it was satisfactorily mastered by slaughter of infected flocks and safe disposal of carcases. In the early part of 1950 the peracute form of the disease was also being brought under very good control in England and Wales, where although outbreaks continued the great majority were in or near the areas to which imported carcases were still being sent.

The record of dwindling numbers of outbreaks gave encouragement that the slaughter policy with ancillary orders controlling the movement of live birds and poultry markets in areas where the disease occurred was proving successful. At that point in 1950 we seemed to be within measurable distance of eradicating infection from the whole country.

NEWCASTLE DISEASE IN GREAT BRITAIN, 1950-58

Up to 5th October, 1950, there had been no recorded case of Newcastle disease in Great Britain for more than five weeks. On that date an outbreak was confirmed in East Anglia in which the symptoms were noticeably milder.

Epizootiology

The source of the infection was not definitely found but the first cases were associated with waste food from a U.S. Air Force base where chicken carcases of U.S. origin were cooked for service personnel. It was known that this milder form of the disease had been prevalent in the U.S.A. for many years and suspicion regarding the route of infection was unavoidable; on the other hand it is possible that the disease might have come from Europe, from which carcases were still being imported, since it was known that in some European countries a milder form of the disease was occurring as well as the peracute form. The disease spread widely in England, notably through the agency of poultry dealers and markets. The symptoms were consistently milder. There was generally a sudden drop in egg production, respiratory symptoms and diarrhoea and at a later stage nervous signs appeared. Mortality was low in adult fowl although it could be considerable in "growers". Experience soon showed that this infection spread more readily to neighbouring flocks than had the peracute infection.

Procedure for dealing with outbreaks

The national poultry industry was now exposed to a disease in which the symptoms were often very slight and could well be mistaken for less serious conditions, and any delay on the part of owners in reporting suspected cases was understandable. Moreover, speedy diagnosis, which is fundamentally necessary if a slaughter policy is to succeed, was made more difficult. As a result infection may have spread to farms contiguous to an outbreak before a definite diagnosis had been made. The situation was reappraised and, although it was realized that eradication by slaughter would be difficult, it was accepted that any method which did not aim at the destruction of the virus at its source offered even less likelihood of success than the policy already being pursued.

The use of the haemagglutination inhibition test. It was necessary to make wide use of the haemagglutination inhibition test in field diagnosis and it is appropriate at this point to describe in some detail the procedure, which has continued since then, for dealing with an outbreak.

On receipt of a report of suspected Newcastle disease the Divisional Veterinary Officer, who is usually in charge of a county, arranges for an immediate investigation by a veterinary officer who visits the premises and makes a diagnostic enquiry. He considers the history, the symptoms, carries out post-

mortem examination of dead or sick fowls and makes a provisional diagnosis. Unless he can exclude the possibility of Newcastle disease, he serves a written notice which bans all movements of poultry out of and into the premises, prohibits the sale of hatching eggs and carcases and the movement of poultry equipment and manure, and forbids human contact with the flock.

Where he suspects the disease he telephones a veterinary officer at the Ministry of Agriculture's head office in London and discusses the case; then either it is confirmed on the clinical evidence alone or arrangements are made to have blood samples sent to one of the Ministry's laboratories from which the results are available on the following day. This procedure does not detract from the ability of the field officer on the spot to make a competent diagnosis but it is done because the veterinary officer at headquarters is knowledgeable on the situation in the country as a whole and is in a position to obtain whatever assistance may be necessary, e.g. consultation with the Central Laboratory.

Negative blood test results do not necessarily mean that the incident is dismissed. In a proportion of cases the restrictions operate until a further blood test, taken after the necessary interval to allow for the development of antibody, has also proved negative.

On confirmation "Infected Place" notices are posted conspicuously at all entrances to the premises to exclude contacts, and straw mats soaked in an approved disinfectant are laid across the entrance roads.

Valuation of stock for compensation. For commercial stock the veterinary officer attempts to make a provisional agreement with the owner on the valuation of the poultry, and provided this agreement is reasonably in line with an accepted scale based on current market prices he proceeds to deal with the case. He notes—or estimates—the number of diseased birds, and the owner is not compensated for these. If agreement cannot be reached, or the stock is of exceptional value, a professional valuer is employed.

The owner is presented with a copy of the valuation form, showing estimates only of the number of birds in each category, their value per head and an assessment of the number of sick birds in each category. Despite his initial agreement, the owner is given 14 days in which he can appeal against the valuation, which if necessary can be referred to legal arbitration, but slaughter of the stock is not held up.

Slaughter and disinfection. If the available farm labour appears to be capable of carrying out slaughter and disposal of carcases and disinfection of the premises with the necessary speed, the work goes ahead. If assistance is required contractors are employed and where necessary they do the whole of the work. In either case the Ministry of Agriculture bears the cost.

All labour operates under the instructions of the veterinary staff. In many cases where fowls are kept on an intensive system (and this applies particularly to broilers) the birds are destroyed by hydrogen cyanide gas. This is always done by approved contractors who are accustomed to the safe use of this material.

As soon as possible after slaughter and before their removal from the poultry houses carcases are counted and soaked with disinfectant approved by the

Ministry of Agriculture as being effective. This serves to reduce the amount of surface contamination, and also renders the carcases unfit for human consumption. Burial in quicklime on the infected premises is the usual method of disposal; mechanical excavators are employed in most cases. Where burial is impracticable the carcases are burned on a surface fire; in built-up areas the carcases may have to be moved to other premises for disposal and this is done in suitable containers.

Feeding-stuffs which have been exposed to infection in poultry houses are buried or burned and payment is made to the owner.

Supervision of disinfection is the responsibility of the veterinary officer, but is usually delegated to technical assistants who visit the premises daily to see that the work is proceeding properly and speedily. The preliminary disinfection is carried out at once and consists of thorough soaking with disinfectant of the whole of the premises to which poultry have had access; workers' outdoor clothing is disinfected at this stage.

When the carcases have been removed the houses and their contents are sprayed with 4 per cent sodium carbonate solution, scrubbed and scraped and again sprayed with soda solution or with an approved disinfectant. Steam under pressure, if available, may be used for cleansing and disinfection. Its use is limited and is not practicable on the average poultry farm, but it can be of value in hatcheries, large-scale brooding units and batteries.

Small quantities of manure, scrapings and litter are buried or burned; larger quantities are stacked in a compact heap which is freely sprayed with soda solution and allowed to heat. In deep-litter systems the litter is stacked within the houses whenever possible. This reduces the risk of contamination dust being disseminated in the neighbourhood.

Overall clothing worn by workers is soaked in soda solution and laundered. Other clothing is fumigated with formaldehyde gas on the infected premises or it may be sent to local authoritity or hospital fumigation depots in the neighbourhood.

Feeding-stuffs in sacks are dealt with either by spraying with formaldehyde solution or by fumigation with formaldehyde gas. Sacks are disinfected with soda solution or fumigant.

Restocking. Restocking is permitted by withdrawal of restrictions either six weeks after slaughter or four weeks after the completion of disinfection, whichever is the earlier. In some circumstances it may be necessary to delay restocking, particularly where there has been a series of outbreaks in the immediate vicinity and the new stock might become infected from local contacts.

Tracing. Information concerning the movement of poultry, carcases and equipment to and from the infected premises and of persons who have been in contact with poultry, is obtained at the time of the initial enquiry and all poultry flocks disclosed in this investigation are examined. Appropriate movement restrictions are imposed for a period of 28 days from the date of contact. Blood samples are taken for the haemagglutination inhibition test.

Flocks in close proximity to an outbreak are particularly vulnerable to lateral spread of infection. Each outbreak is therefore looked at in the light of

numbers of infected birds, density of poultry population in the district, how long disease has been present, system of husbandry and other factors. Contiguous flocks likely to have been exposed to infection are valued and slaughtered at once. This does not apply to particularly valuable flocks which are kept under observation. Restocking on these premises is not permitted until the premises on which the outbreak occurs is freed from restrictions. Blood samples are taken for the haemagglutination inhibition test from each flock slaughtered as this may reveal undisclosed infection and a possible origin of the primary outbreak.

Movement restrictions. All poultry within half a mile of the infected premises are placed under movement restrictions for 28 days. The period may be extended if further outbreaks occur. All flocks within quarter of a mile are inspected by veterinary officers and blood samples are taken for testing.

It has been found that this method of dealing with an outbreak is speedy and efficient and in all cases includes a thorough investigation to find the origin of the infection.

In January, 1951, nation-wide publicity was given through organizations of the poultry industry, the national agricultural press, the B.B.C. and the veterinary profession about this subacute form of disease. The symptoms were described and precautions which poultry keepers should take were outlined. There are a number of diseases of cattle, sheep and pigs which are notifiable in Great Britain, and in our experience the owners of livestock generally respond well to their responsibility. Widespread infection had occurred through poultry markets, and restrictions on the movements of poultry and the holding of markets were applied in the eastern counties and in several other areas in England and Wales. An increasing number of suspected cases were brought to the attention of the Ministry by owners, and more were found by tracing sales and movement of fowls from known outbreaks. This exercise resulted in many cases being confirmed, but by April 1951 the situation had been brought under good control.

Importation of Poultry Carcases Order. In May 1951 the importation of poultry carcases from any country where Newcastle disease was prevalent was prohibited, and when, after some months, carcases from these countries had been cleared from cold stores it could be assumed that infection had ceased to be imported. The problem then was to contain and eradicate infection already in the country. The success obtained in eradicating the disease from many parts of England and Wales and from Scotland gave reasonable hope that complete success might thus be achieved.

Towards the end of 1951, Newcastle disease was confirmed in poultry which had been exhibited in the National Poultry Show in London. All the birds which had been entered at the Show were traced, examined and submitted to the haemagglutination inhibition test. In 1951 844 outbreaks were confirmed. and of these only 28 were of the peracute type, judging by symptoms and mortality. In 1952 and 1953, although the number of confirmed cases ran at 498 and 978 per year, only about 20 per cent were foci of primary infection and large areas of the country remained free of the disease.

Haemagglutination Inhibition Test Survey. In 1953 a survey was carried out by the haemagglutination inhibition test of a representative number of blood samples in flocks situated in eight counties where the disease had been particularly troublesome. The total population of poultry in the flocks sampled was over half a million. The aim was to see whether there was evidence of continuing widespread infection. Positive blood samples were found in 2 per cent of the flocks but wider sampling in these flocks, to include different age groups, carried out over a period, along with close investigation of recent movements and purchases of poultry, brought no evidence of widespread undisclosed disease in counties where it might possibly have been expected.

"*Clean areas*". This survey, along with the experience that it had been possible to protect Scotland by a statutory ban on the entry of live poultry, day-old chicks and hatching eggs from England and Wales, led to the introduction early in 1954 of a new conception of movement control: the establishment of "clean areas" into which the movement of birds could be prohibited. A "clean area" consisting of the whole of Wales and several counties in the west of England was declared. As the situation improved elsewhere in the north and south-west of England, other counties were added to it. The movement into the clean area of all live poultry other than day-old chicks was prohibited. This was a realistic policy of pushing back the frontiers of the disease and thereby allowing a much greater effort to be concentrated in those counties where it continued to appear, notably in the south and south-east of England. It was possible at the same time to tighten the legislation governing the movement of live fowls; for example poultry dealers and auctioneers were required to keep records of their sales of birds by which vendors and purchasers could be traced quickly by veterinary officers investigating an outbreak. After several outbreaks, which were seeded from contiguous counties when the "clean area" was declared, had been dealt with and the premises restocked there was no further case of Newcastle disease recorded in the "clean area" for nearly two years.

In 1954 the situation was under reasonably good control. During the year 795 cases of Newcastle disease were confirmed and of these 75 per cent were reported by owners. This was a considerable improvement on previous experience with the subacute form.

In the early part of 1955 the number of outbreaks steadily declined but in the second half of that year there were several notable incidents. For example, one infected unit dispersed growing birds widely in England and as a result 108 secondary outbreaks were disclosed. After a breach of the regulations there was also an invasion of the clean area in Wales which resulted in widespread infection through markets and the declaration of nearly 200 outbreaks before it was stamped out. Although there were 906 outbreaks in the year only 160 were primary cases.

Infected Areas Restrictions Order. In 1956 the Fowl Pest (Infected Areas Restrictions) Order was introduced; this allows the Ministry to prescribe areas from which live poultry may not be moved and within which movements, broadly limited to fowls for immediate slaughter, may only be made under

licence. This Order is applied to an area when the circumstances of an outbreak or series of outbreaks shows that spread of disease may be expected, e.g. when there is heavy infection in a district or when there is a number of apparently unconnected cases in an area of dense poultry population, or where there is evidence of infection in poultry markets. Store poultry markets, shows and exhibitions of poultry are prohibited. The Order also requires the disinfection of egg lorries and equipment belonging to egg-packing stations, and defines specific precautions to be taken by chick sexers. Prior to the introduction of this Order restrictions on the movement of poultry could only be applied by the veterinary officer in flocks in a limited district in relation to a confirmed case.

Poultry Premises and Vehicles Disinfection Order. In 1955-56 circumstantial evidence showed that a large number of primary cases were caused by poultry slaughterers or their agents visiting farms and handling culls. In many cases it was in the section of the flock in which birds had been handled that the disease first became apparent. The centres of this trade are in London and other large towns, and a survey carried out by London County Council showed that the standard of hygiene was very low; live birds were brought together in large numbers and there was ample opportunity for the multiplication of virus. The Poultry Premises and Vehicles Disinfection Order was introduced and it permitted the service of notices where, on inspection, premises or equipment were found to require thorough cleansing. In the first year over 12,000 visits were made by Ministry or local authority staff and over 2,000 notices requiring cleansing and disinfection were served.

The subsequent records showed a reduction in the number of primary cases, particularly in the counties around London. In 1956 the holding of sales of poultry in auction markets of birds other than for immediate slaughter was prohibited between October and December, since experience had consistently shown that the incidence of disease increased in the last quarter of the year, partly because of the increased movements of poultry. This prohibition on markets in October to December has been maintained in subsequent years.

In 1957 the "clean area" system of control was abandoned. It has been successful in keeping a large part of the country clear of infection, but consultation with the poultry industry showed that the policy was severely restricting normal trading and the (Infected Areas Restrictions) Order had proved to be an effective method of containing disease in areas where it was most troublesome, thus enabling the veterinary staff to intensify their efforts to eradicate it.

Newcastle disease in Lancashire

An important highlight at this time in the fight against Newcastle disease was the experience in Lancashire. In this county, the recorded poultry population is over eight millions on holdings of one acre and above. The actual population is probably nearer 12 millions. Most of the poultry development is in the central area of the county and consists chiefly of commercial laying stock, most of which is housed in battery or deep-litter intensive systems.

There are some very large units but generally the holdings are small in relation to the number of birds. In the most densely populated areas poultry is the only livestock enterprise, and frequently villages are joined by chains of contiguous poultry holdings. The number of birds on a holding varied from a few hundreds to several thousands. The majority of owners purchase their replacements as day-old chicks, brood them indoors to three to four weeks of age, rear them to five or six months in small paddocks and then move them to permanent laying quarters in the intensive houses. At the end of their laying period the fowls are sold to a poultry slaughterer for table purposes.

It was in this area that Newcastle disease appeared in the autumn of 1955 and resulted in 146 outbreaks before the end of the year. There was a marked improvement in the early months of 1956 but in November and December of that year nearly 300 cases were confirmed. "Area" restrictions had been imposed and disease was remarkably well contained within the area. Meetings were held with representatives of the industry to encourage better reporting of disease and to cut down personal movements from farm to farm. An analysis of 386 outbreaks showed that 114 secondary cases had occurred on premises contiguous to the outbreaks, a further 157 were situated within quarter of a mile and 58 within one mile. It was therefore decided to extend the slaughter procedure and in addition to all fowls on the infected place being destroyed those in contiguous holdings were also slaughtered and the haemagglutination inhibition test was applied extensively throughout flocks within a wider perimeter.

At the same time, the diagnostic procedure was speeded up so that the great majority of cases were confirmed on the history and clinical findings without a wait of up to 24 hours for the results of the blood test. Constant efforts were made to make owners familiar with the early symptoms of the disease. This forthright action had the full support of the local poultry organizations and consequently it was possible to get at the foci of infection more quickly, so that by the early months of 1958 the epidemic had been conquered. Some months later, blood samples were taken in 247 flocks in the area in which eradication work had been going on for so long, and positive results were obtained only in three flocks. Although none of these had a history of clinical disease, they were slaughtered. That was over two years ago and there has been no recrudescence of disease in that part of Lancashire. That the disease is absent is supported by the fact that many reported cases have been investigated and found not to be Newcastle disease. However, outbreaks have occurred in other parts of Lancashire which had no connection with the previous epidemic.

The Effect of the expansion and changing structure of the industry, 1959-60.

Although there was recurrent infection during 1958 in the eastern counties, where the subacute form of the disease had started in 1950, the greater part of England and Wales was free from primary cases. A good deal had been learned from the experience in Lancashire.

In 1958 the number of outbreaks—759, of which 228 were primary cases—was the lowest recorded for five years. Nevertheless, about this time application of the slaughter policy was becoming more costly because of the changing trends in the poultry industry. There was an expansion in the laying fowl population, an increase in flock size, an increase in intensive systems of management, the emergence of large organizations, and the development of the broiler industry from five million broilers in 1953 to about one hundred millions in 1959. This section of the industry is highly organized, with the evolution of the group system involving distribution of stock, collection, slaughter and marketing of carcases. This growth of the industry and particularly the increase in intensive poultry rearing has increased the difficulties of disease control and in addition has made the bill for compensation much more costly, because of the rapid turnover in broilers, so much greater even than the already rapid turnover in other classes of poultry flocks. In 1951, 400,000 fowls were slaughtered at a cost of £496,000; in 1958 1,300,000 were destroyed at a cost of £1,280,000.

In the early months of 1959 the disease was almost entirely confined to one county in the east of England. In the autumn it struck broiler units in the west Midlands. Due partly to the massive infection and also to the fact that some of the cases were not reported, there was widespread dissemination of virus. It was difficult even for an augmented veterinary staff to keep pace with diagnosis, slaughter and the investigation of outbreaks. Disease in broilers and other intensively housed poultry then spread to the east Midlands and the eastern counties.

Infected area restrictions were applied widely and no doubt prevented even a greater spread of the disease but this was undoubtedly the most serious epidemic in twelve years' experience. It was the first time the disease had seriously affected the expanding broiler industry; and when infection reached one section of an enterprise which had scattered units several miles apart, it was carried by indirect means—visits by suppliers, transport or transfer of equipment led to extensive infection in the areas under restrictions. Nor was the spread of disease easily stopped by slaughter of poultry in contiguous holdings and those belonging to employees.

Wind-borne Infection. A new and important danger of spread was involved for it became quite clear that the extractor fans in the mechanical ventilation systems carried wind-borne infection. A sizeable proportion of the Ministry's veterinary staff was engaged in the epidemic until the spring months of 1960 when it was got under control. In 1959, 2,062 outbreaks were confirmed, nearly 5,000,000 birds were slaughtered with compensation of nearly £3,500,000 Of all the fowls slaughtered 49 per cent were in broiler units.

In the first six months of 1960 there were 1,321 outbreaks and 3,700,000 birds were slaughtered at a cost of over £2,300,000 and the proportion of broilers among birds slaughtered was 60 per cent.

CONCLUSIONS

Since 1950 the Ministry of Agriculture has never had any other view than that

this disease would be very difficult to eradicate, but it is believed that a slaughter policy with full control on the movement of poultry, control of dealers, and poultry markets—and this must be a integral part of a stamping-out policy —is the only method that offers any hope of eradication. From what is known of the experience of many countries which have adopted palliative methods of control, it seems that although their poultry industries are able to conduct their business without irksome restrictions they will have to apply some form of immunization for the foreseeable future and at the same time, they will have to live with a varying incidence of Newcastle disease.

In our experience, there is a great deal to show on the credit side. The peracute form has been eradicated; Scotland has been kept reasonably clear of infection and when it has occurred there our policy has been effective. The epidemic in Wales was cleaned up in 1956 and that country has been kept clean. When our methods were tested almost to the physical limits in Lancashire, they were successful in eradicating what certainly appeared to be well-lodged endemic disease in that county. On the general situation in England, the disease has been confined mainly to the eastern counties. Even in 1959, for example, in 25 counties in England and Wales no primary case was recorded. This is notwithstanding the fact that sporadic outbreaks must be expected either directly from even a small number of unreported cases, or indirectly from these cases via the medium of improperly cooked swill containing poultry offal. It appears inevitable that some infected carcases reach cold store and when they are released they can become a fruitful source of virus to reinfect, many months afterwards, an area that has been freed from the disease. It has been proved unequivocally that evisceration does not provide sufficient protection. It is understandable that it is much more difficult to apply controls to poultry than to large animals and while the policy has the full support of the British poultry industry there are some owners who have less at stake than others and who have consequently less interest in disease control.

It is also known that Newcastle disease sometimes shows milder symptoms in turkeys than in fowls and that ducks may have a transient sickness which may go unobserved. The virus has been recovered from jackdaws and recently from a house sparrow; sizeable outbreaks in pheasants kept close to domestic poultry have been dealt with, but there is no evidence that these species provide substantial reservoirs of infection.

Experience in the winter of 1959/60 put our method of dealing with Newcastle disease to a much greater test, mainly because of the recent developments in the poultry industry, and certainly the Government has taken note of the greatly increased costs. Therefore, in spite of our belief that the system employed is the only method that could achieve eradication, we welcome the setting up of a Committee of Inquiry. It is now a question of whether this level of expenditure is acceptable or whether other methods with less cost to the Government are preferable. We make no suggestion that our methods have virtue for application in circumstances other than those in Great Britain.

SUMMARY

An historical survey of Newcastle disease in Great Britain since its first recognition by Doyle in 1926 is given.

The epizootiology of the legislative and other procedures adopted in the attempt to eradicate the epizootic which started in 1947 are described in detail. Despite the experiences of 1959/60 there is a great deal to show on the credit side for the policy adopted. The peracute type of the disease has been eradicated. Poultry stocks in Scotland have been protected, whilst Wales and many counties in the west and north of England have similarly been kept clear.

As a result of recent trends in the expansion of the broiler industry the control of the disease has presented considerable difficulty in certain areas, notably East Anglia, and the policy is at present under review by a Committee of Inquiry.

(*Received for publication, 1 March 1961*)

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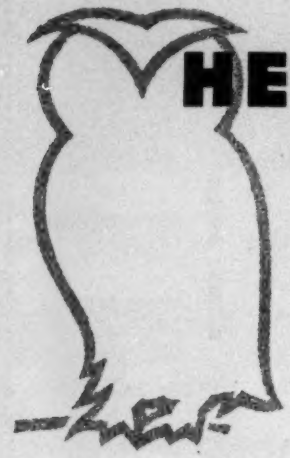

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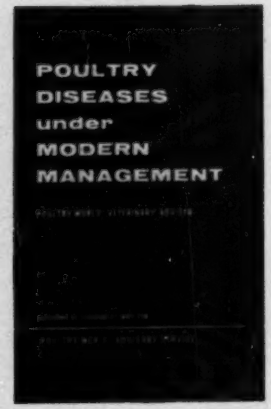

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CONTROL OF NEWCASTLE DISEASE AND INFECTIOUS BRONCHITIS BY VACCINATION

By J. Hoekstra
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This subject is complex and extensive and it will be impossible to deal with all aspects of the problem in the space available. The discussion of it is therefore restricted to the more important experiences which have been acquired in the Netherlands in vaccination programmes against Newcastle disease and infectious bronchitis, both experimentally and in the field.

These two conditions have much in common. Both are more or less primary respiratory diseases, it is often difficult to differentiate them clinically, and patho-anatomically the typical inflammatory changes in the air sacs, especially in chicks, are almost identical. The poultry farmer regularly confuses the two diseases and this is one reason why he prefers a combined vaccine. If possible he would prefer to use an "all-risk" vaccine and the matter of multiple vaccines will be referred to later.

NEWCASTLE DISEASE

This disease first appeared in the Netherlands in 1950 in a severe form and there were very high losses, especially in 1951. At the beginning an effort was made to eradicate the disease by official control measures. We did succeed in containing the disease to some extent but not beyond a definite and rather constant level. There then developed, as it were, a certain biological equilibrium between the virus on the one hand and our official control measures on the other, and the reasons why it was impossible to obtain complete eradication were fairly clear.

In the first place there was an increase of mild or even subclinical cases; some of these could not be recognized and were not reported to the authorities. It must also be added that compulsory notification and slaughter was unpopular, particularly in mild outbreaks, unless they occurred in broilers at a time when prices were very low. A factor to be borne in mind is the high density of poultry in the Netherlands. For example there are seven agricultural holdings per square kilometre (18 per square mile), on which poultry are maintained, and in some poultry regions double that number. Under these circumstances it was impossible to obtain watertight isolation of affected farms.

After some years it was clear that eradication could not be achieved by hygienic measures only and that the disease was endemic and would remain so. Bearing this in mind, we had to decide how to live with this disease in the best way and limit the economic damage to the minimum. In the absence of effective therapy only vaccination remained, but a choice had to be made between living and dead vaccines. Dead vaccines had the advantage that dissemination of the virus in the country could be prevented. On the other hand there were

the disadvantages that the immunity provoked by killed Newcastle disease vaccines was of rather short duration, whilst their preparation is more expensive than that of the living vaccines. The main difficulty, however, is that dead vaccines could only be administered individually by injection by veterinary surgeons. This is much too cumbersome and expensive a procedure, as it would be necessary to inject tens of millions of animals annually. Because of these large numbers and the relatively small value of the animal concerned, it was thought to be impracticable to carry out vaccination on individual birds.

With living vaccines the situation is much easier. Their production is cheaper and the vaccine is practically always administered via the drinking water. The disadvantages of the living Newcastle disease vaccine, which will be discussed later on, are slight, provided that a good vaccine strain is used.

For vaccination against Newcastle disease in the Netherlands, only the Hitchner B1 strain is used and ample experience with this vaccine has been obtained both in the laboratory and in the field. Each batch of vaccine was tested in the laboratory on a number of experimental chicks, and when these separate tests were totalled the pathogenicity of the strain was shown to be slight. There were no deaths in a total of 118 vaccinated chicks of approximately one week old. One chick, however, became permanently lame. Regularly "takes" could be observed. The vaccinated chicks were somewhat lazy for a couple of days during the second week and sneezed slightly. A total of 95 chicks were challenged with fully virulent virus three to four weeks after vaccination; only one chick died and the remaining 94 showed no symptoms of the disease. In the control (untreated) groups there was a constant mortality rate of at least 90 per cent within five to seven days.

In addition to these excellent laboratory results which could be constantly reproduced, there are results from the use of the Hitchner vaccine in the field. In the first place, let us consider the possible effects of pathogenicity, for occasionally complaints reach the producers of the vaccine of too severe and harmful vaccination reactions. This occurred two years ago, for example, in Gelderland, one of the most intensive poultry districts. Complaints were received of mortality amongst the vaccinated flocks and that a faulty batch of vaccine had been put on the market. This caused much consternation and justified a thorough examination on the spot. The following facts came to light:

On 19 farms, chicks from one to two weeks old had been vaccinated. The average mortality caused by the vaccination amounted to 1·8% (varying from zero to 5·2%). On 12 farms with chicks of three weeks old the losses varied from 0—4% and on eight farms with chicks of four to seven weeks old the mortality averaged 0·7%, ranging from zero to 1·7%. All deaths occurring during three weeks after vaccination were included in these totals and may have included deaths from other causes. These data related to approximately 24,000 chicks in a district where farmers raised many objections to vaccination, yet in the same district many cases of spontaneous Newcastle disease occurred at the same time. Nevertheless, in the course of some years, only in one case was there any mortality from vaccination when ten per cent or more of these chicks had been vaccinated. These rare cases can usually be attributed to other factors,

for example, intercurrent disease, or faulty housing or management.

The Hitchner vaccination of broilers needs separate discussion. In such flocks the situation is difficult, for where rapid growth is concerned people make very high demands on their broiler chicks. Housing is very intensive, while ventilation problems are only partially solved. Under these circumstances vaccination is often not well tolerated, especially in chicks of one or two weeks of age.

Broilers can only be vaccinated without risk if three conditions are fulfilled: (1) the flock must be in perfect condition and good health; (2) husbandry and housing have to be at the optimum; (3) the chicks must come from vaccinated stock and have acquired a parental immunity.

Undesirable harmful "takes" sometimes occur in laying hens vaccinated for the first time. This matter was investigated by van Schaik (1959) in one of the Dutch islands where at first farmers were not accustomed to vaccination and where mass vaccination had been carried out after an outbreak of Newcastle disease. Flocks of laying hens vaccinated for the first time showed a drop in production averaging 25% for a period of three weeks, after which production increased again. Such a serious decline in production, however, is not general, and is the exception rather than the rule. Earlier we had noted that in 15% of the laying flocks vaccinated for the first time a decline in production occurred. As a rule this was not more than 10 to 15% and lasted for only one or two weeks. Apart from that, the Newcastle disease outbreak in the island in question was eliminated in a very short time. It is now clear that primary vaccination is not suitable for laying hens, but there are no other disadvantages to vaccination.

Immunity produced in the field by the Hitchner vaccine has been very good. It is true that immunity sometimes is less effective than with well-executed and controlled laboratory vaccination, but at the same time highly virulent strains of Newcastle disease are not so frequently encountered in the field. As a matter of fact, outbreaks of Newcastle disease in regularly vaccinated farms are very rarely reported. Quarterly revaccination is required, because the Hitchner drinking-water vaccine does not give a lasting immunity (it lasts about two to three months in young chicks and three to four months in adults).

Finally attention should be drawn to some technical requirements for successful vaccination with the Hitchner strain. The virus titre in the drinking water prepared for vaccination should be high and perfectly standardized. Low titres yield irregular results. Furthermore, on examination, Hitchner strains of different origins showed diverging characteristics. These strain differences are, for example, responsible for deviations in neuropathogenicity after intercerebral injections in day-old chicks. This fact can be used when the standardization of vaccines of different levels is carried out. As a rule, the vaccines with the disadvantage of a somewhat higher pathogenicity give optimum immunity. Unfortunately, the poultry to be vaccinated cannot be likewise standardized.

INFECTIOUS BRONCHITIS

This disease has occurred in the Netherlands since 1947. During the first years

it was seen mainly as a mild disease of young chicks, but later on laying hens were also affected, often with serious economic consequences resulting not from mortality, which seldom occurs in adult birds, but from the damage caused by the severe and lasting depression in egg production.

Infectious bronchitis infection spreads very quickly and in some years 85% of the poultry farms in different regions have been affected. This disease is even more difficult to control than Newcastle disease. Official control measures have not the slightest chance of success and have not even been considered in the Netherlands. This is easy to understand when we remember that the infectivity of infectious bronchitis virus is extremely high and the clinical picture very varied. Occasionally serious respiratory symptoms can be observed, but in other cases the course of the infection is very mild or nearly sub-clinical. Vaccination with live virus vaccines is almost the only possible method to use for the control of infectious bronchitis. Dead virus vaccines have not been developed so far for the control of this disease.

However, vaccination with live virus vaccines against infectious bronchitis has proved to be a difficult problem. Too much or too little can easily be administered. Vaccines prepared from a potent vaccine strain will induce a particularly good immunity but they have the disadvantage of being more pathogenic. On the other hand vaccine strains which produce only poor reactions provoke, as a rule, only poor immunity, whilst the more potent strains produce better and more consistent reactions.

A slight but rather general vaccination reaction in the flock should preferably be seen, whereby the chickens exhibit moist or dry sneezing but show no nasal discharge as in coryza, and no decline in general condition. In those circumstances "takes" are satisfactory and indicate a good immunity. When no "takes" are observed after vaccination, then immunity is uncertain; occasionally immunity may be fairly good and sometimes it is completely absent.

Whilst the vaccines can be standardized the poultry cannot, nor can a long list of contributory factors which can exert a big influence on the course of the vaccination reaction. Especially important are ventilation, the poultry-house temperature, ammonia fumes, secondary infections and a certain degree of parental immunity. The complexity of these different factors often influences the course of the vaccination reactions more than the vaccine strain itself.

It follows from this that the effect of an infectious bronchitis vaccine cannot be determined on the basis of laboratory tests only and ample experience in the field is necessary to determine and judge the advantages and disadvantages of certain types of vaccine.

One of the first vaccines used was an indigenous, rather mild strain, which after primary isolation underwent 52 passages in embryonated chicken eggs. Although this strain when applied as a vaccine in laboratory tests gave very good results, it was decided to carry out field trials together with control visits and investigations on the farms, in order to obtain further information. In this way data relating to a total of 150,000 chickens and hens were obtained; the most important details of which are as follows:—

The vaccination reactions in the various flocks varied widely from practically no reactions to moderate respiratory disturbances, together with general symptoms in the form of sluggishness and inappetence. Mortality among younger groups of chicks of one to three weeks of age averaged 2 to 3%, decreasing according to increasing age. In six-week-old chicks the mortality was only 1%. Mortality in vaccinated pullets (two to four months of age) was negligible.

These results were not unsatisfactory and farmers did not object to such mild reactions in controlling such a serious disease. However, these post-vaccinal mortalities are average figures and although in most poultry farms the mortality was much lower than the average, on a few other farms it was considerably higher, rising in exceptional cases to 10 per cent. When we investigated these problem flocks on the spot, we found that other factors, such as faulty ventilation or other coexisting diseases, could be held responsible for the excessively severe vaccination reactions. It was equally clear that the poultry farmers involved derived little consolation from this knowledge!

In the field less healthy flocks are sometimes seen and vaccination methods have to be adjusted to the circumstances. Sometimes it has been shown that vaccination with this strain in broilers causes a slowing down of growth, which is not recovered by market age. The vaccine strain in question is therefore now restricted for use with young breeding stock of three to four months of age, since it is not suitable for young chicks. However, its immunizing power is very high. In laboratory experiments it was found that three weeks after vaccination, high serum neutralization titres were produced, reaching a maximum in eight to ten weeks, and thereafter declining to low or negative titres at about four or five months after vaccination. The immunity lasted for approximately one year. An enquiry carried out on 221 vaccinated flocks in infected regions showed only one spontaneous outbreak of infectious bronchitis of importance.

To enable young chickens, also, to be vaccinated safely, a mild infectious bronchitis vaccine was developed by passaging the same strain 120 times through embryonated chicken eggs. This resulted in a further reduction in pathogenicity and produced much slighter clinical "takes" in vaccinated chicks, yet its immunizing power remained satisfactory.

The reduction in pathogenicity was shown by the fact that autopsies on chickens killed three weeks after vaccination with the original vaccine strain H.52 showed in 16% of the cases evidence of recovered or partially recovered inflammatory lesions of the air sacs. This was reduced to 2% when the mild strain H.122 was used.

Some years ago a commercial organization put on the market a mild infectious bronchitis vaccine, using Jungherr's strain 82828 in its 45th egg passage. This strain belongs, as does ours, to the Massachusetts type. In the field, farmers now use a mild strain vaccine for the vaccination of young chicks, or for laying hens in emergency. However, for replacement stock of three to four months old, a more potent vaccine is usually preferred.

COMBINED VACCINES

The first vaccination against infectious bronchitis at the age of about three weeks is often combined with Newcastle disease vaccination, and the use of combined vaccines deserves comment. Poultry farmers generally are very interested in the possibility of combining the two vaccines against Newcastle disease and infectious bronchitis, especially since they cannot easily differentiate the two diseases and wish to be protected against both. Combined vaccination would lighten the sometimes overcrowded vaccination schedule and save labour.

Theoretically, the combining and administering of two vaccines at the same time is of debatable value. One must bear in mind the danger of a cumulative effect of the pathogenicity of Newcastle disease and infectious bronchitis vaccines. Furthermore, Hanson (1956) and others have drawn attention to the fact that an interference phenomenon between Newcastle disease and infectious bronchitis virus strains cannot be ruled out. These questions, however, are not easily solved by laboratory experiments and it is not possible to say whether or not, or to what degree, the combination of both vaccines in the field will produce satisfactory results. In a limited number of recent laboratory experiments the combination did not influence the final results. In other words, the combination worked as well as the separate administration of the two vaccines. One could imagine, however, circumstances in the field which would lead to a less fortunate result. After a combined vaccination it has been impossible to get a clear picture of the cause of the resultant "takes". Both vaccines or only one of them may have been responsible and to the author's mind this uncertainty is a distinct disadvantage. Non-vaccinated farms threatened by both diseases at the same time have of course no choice. They should vaccinate with combined vaccines as soon as possible.

If it is asked whether these mass vaccinations in the Netherlands have any disadvantages, the answer must be in the affirmative and this is realized only too well. For example, too severe "takes", although fortunately rare, are accompanied by mortality in young chicks and a reduction in the growth rate, and by heavy drops in egg production in laying birds; sometimes secondary infections are observed. Conversely, after very slight "takes" or after no reaction at all, the flock may lack immunity. Furthermore, the simple fact of having applied the vaccine will set the poultry farmer's mind at rest, with the consequence that he neglects the necessary hygienic precautions. The vaccines, particularly the infectious bronchitis vaccines, then spread to other groups of unvaccinated poultry which may become vaccinated free of charge!

We could even consider these mass vaccination programmes as a kind of artificial slight epidemic, roaming the country at regular intervals, yet acceptable, because the accent is on "slight" and not on "epidemic".

Mass vaccination in Holland then, is not satisfactory, but the alternative is even less so. That is to say, vaccination is preferable to repeated serious outbreaks of spontaneous Newcastle disease and infectious bronchitis.

Finally, comment should be made on the quality of the vaccines. Extensive

control measures are required to be sure of a good product and this cannot be done without ultimate government control. Complete and efficient control, however, is laborious and expensive; not only do different and successively produced batches of vaccine have to be examined, but the control must begin with a careful investigation of the vaccine strains to be used, and with a study of their characteristics. In this connection it should be noted that Jansen and Richter (1959) pointed out that an expensive institute for that purpose could probably best be founded by a group or combination of countries, for viruses and live vaccines are too apt to neglect national frontiers.

SUMMARY

An attempt to eradicate Newcastle disease in the Netherlands by official control methods failed.

The paper describes the subsequent policy adopted, in which a live virus vaccine (Hitchner B1 strain), administered in the drinking water, was used. Provided the vaccine is applied at three-monthly intervals, excellent protection is obtained. In broilers severe vaccination reactions may occur when intercurrent disease is present, whilst a slight decline in egg production may occur in pullets vaccinated for the first time.

One infectious bronchitis vaccine used is prepared from an indigenous field strain of the virus attenuated by some 50 egg passages. The strain is too pathogenic for use in young chicks and is restricted to the vaccination of three to four-month-old birds. For young chicks and for laying fowls a milder vaccine produced by further repeated egg passages of the same strain is used.

A limited number of experiments have shown that the use of a combined Newcastle disease/infectious bronchitis vaccine was as effective as either vaccine given separately. The method, however, is not entirely free from hazard and the advantages and disadvantages of a combined vaccine are discussed.

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AETIOLOGY AND CONTROL OF CHRONIC RESPIRATORY DISEASE

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This report deals with two aspects of chronic respiratory disease: its aetiology and a proposed plan for its eradication.

THE AETIOLOGY OF CHRONIC RESPIRATORY DISEASE

Infections of the respiratory system of poultry can be classified into four categories:—

Viral infections: myxovirus infection, Newcastle disease, infectious bronchitis, infectious laryngotracheitis and fowl pox.

Microbial infections: infectious coryza (*Haemophilus gallinarum*), pasteurellosis and pullorum disease.

Neo-rickettsial infections: ornithosis-psittacosis group.

Chronic respiratory disease (and infectious sinusitis in turkeys). This is the main subject of this report, since its aetiology is still unresolved.

This latter name, which is too indefinite to be satisfactory, refers to a subacute, irregularly contagious disease, the characteristics of which are as follows:—

(1) *Symptoms.* In young chickens, chronic respiratory disease starts with an inflammation of the upper parts of the respiratory tract and of the mucous membranes anatomically related to these parts, i.e. a coryza with serous or sero-mucous nasal discharge causing sneezing, sinusitis, conjunctivitis and an inflammation of the trachea, accompanied by gasping and coughing. After or even during this first period, the inflammation reaches the lower respiratory tract, producing rather vague symptoms consisting of coughing and accelerated respiration. In all cases the growth rate is more or less retarded so that serious economic losses result, even though the mortality, if any, is low.

In laying hens, chronic respiratory disease causes a fall in egg production and a drop in the number of eggs hatched, whilst the viability of the newly hatched chicks is lowered.

(2) *Autopsy findings.* The lesions in affected birds consist of an inflammation of the upper respiratory tract, with thickening of the nasal and sinusal mucous membranes and sometimes congestion and petechial haemorrhages in the trachea. Very often a mucous or caseous exudate is found in the trachea and in the air sacs, the walls of which are thickened and opaque. Sometimes an exudate is found in the lungs, the pericardium, on the surface of the liver, the peritoneum and the ovaries. Histological examination shows only a lymphoid infiltration in the mucous membranes, this reaction with the formation of granulomas being common among birds.

(3) *Aetiology.* The approach to the aetiology of chronic respiratory disease has been marked by some important discoveries. Nelson (1936*a*, *b*, *c*) described three types of fowl coryza, a bacterial form due to *Haemophilus gallinarum*, a coryza in which the nasal exudate, stained by Giemsa's method, contained very small coccobacillary bodies (also known as "Nelson's bodies"), and mixed infections of both agents. Delaplane and Stuart (1943) described a "chronic respiratory disease" of the chicken, cultivated the causal agent on embryonated eggs, and concluded that it was a virus. Further investigations characterized its pathogenic properties and demonstrated that it was also responsible for infectious sinusitis in turkeys. Later, Markham & Wong (1952) succeeded in cultivating the chronic respiratory disease agent on cell-free media and suggested its inclusion amongst the pleuropneumonia-like organisms (P.P.L.O.) There is now convincing evidence that these P.P.L.O's are identical with Nelson's coccobacillary bodies.

Fahey and Crawley (1954) isolated a virus from cases of chronic respiratory diseases in Canada. This virus is different from those previously isolated and may play only an incidental role, since other workers have been unable to incriminate this virus in chronic respiratory disease outbreaks. Nevertheless, Crawley (1959, personal communication) claims that chronic respiratory disease is due to the combined action of a P.P.L.O. and a natural or vaccinal virus such as Newcastle disease, infectious bronchitis or fowl pox.

The cultivation of P.P.L.O's and the serological reaction of infected birds have been investigated by many workers and in 1956 Edward and Freundt suggested that they should be regarded as a special family, the Mycoplasmataceae, with the single genus *Mycoplasma*. The species considered to be the agent of chronic respiratory disease is *Mycoplasma gallisepticum*.

Nevertheless, even if *M. gallisepticum* is pathogenic on its own account, microbial secondary infections are commonly associated with it and can even reproduce by themselves the clinical symptoms and lesions of chronic respiratory disease. Moreover it seems that stress factors play an important role, so that the aetiology of chronic respiratory disease is complex.

It is therefore necessary to consider (1) the P.P.L.O. problem, (2) other specific bacteria, and (3) stress factors.

(1) *The P.P.L.O. problem.* The type species of the pleuropneumonia-like organisms is the microbial agent of contagious bovine pleuropneumonia discovered by Nocard, Roux, Borrel, Salembeni and Dujardin-Beaumetz (1898). Even today such micro-organisms cannot be satisfactorily defined. Sabin (1941) claims that the two main criteria of identification are the ability of the organisms to grow in cell-free media with the development of polymorphous, globular, filamentous or ring-shaped corpuscles and filterable bodies 125/250 microns in size, and the formation of minute colonies from 10 to 600 microns in size on suitable solid media.

The cultivation of P.P.L.O's is difficult since their nutritional requirements are still uncertain. Most of them require blood serum, cholesterol and deoxyribonucleic acid. They grow easily in embryonated eggs and tissue cultures, but the use of embryonated eggs for laboratory work may not always be

acceptable unless it can be guaranteed that the eggs came from non-infected hens. Furthermore, it is difficult to define the growth of P.P.L.O's in eggs.

The inoculation of avian P.P.L.O's into rabbits can be used to obtain referential agglutinating sera which are useful for identifying the different serotypes isolated, two of which will be discussed.

By 1956, experimental inoculation with pure cultures of P.P.L.O's from clinical cases of chronic respiratory disease showed that a distinction had to be made between strains capable of reproducing the disease and strains without marked virulence; hence the separation of P.P.L.O's into two groups, pathogenic and non-pathogenic (Adler & Yamamoto, 1957; Adler, Yamamoto & Berg, 1957; Adler, Fabricant, Yamamoto & Berg, 1958; Chu, 1958; Chu & Newnham, 1959). Edward (1960) described three species, one pathogenic, *Mycoplasma gallisepticum*, and two non-pathogenic, *M. gallinarum* and *M. iners*. Yamamoto & Adler (1958) separated at least five serotypes, the two main ones being labelled "S.6," for the pathogenic and "C" for the non-pathogenic. The former corresponds to *M. gallisepticum* and the latter to *M. gallinarum*. Confusion has been caused in the literature by the misuse of the name *M. gallinarum* for the pathogenic agent of chronic respiratory disease.

Certain differential characteristics can be defined to distinguish the two species: *M. gallisepticum* grows slowly, small visible colonies without a central nipple appearing on solid media after five or six days. The micro-organism is regularly coccobacilliform; it slowly ferments glucose and haemagglutinates fowl erythrocytes.

M. gallinarum grows readily and rapidly within two days, giving larger colonies with central nipples visible to the naked eye; the organisms are polymorphous; glucose is easily fermented and it does not haemagglutinate red cells.

The latter organisms are common in the upper respiratory tract of the fowl, together with other bacterial species, and this makes it difficult to isolate *M. gallisepticum* in culture media from tracheal swabs, for if the growth of bacteria is inhibited by agents such as penicillin or thallium acetate, *M. gallinarum* grows rapidly and spreads over the whole surface of the nutrient agar, or invades the whole broth, so that *M. gallisepticum* colonies cannot be distinguished. It is necessary therefore to use media that are dysgenic for *M. gallinarum* and which encourage the growth of *M. gallisepticum*. At present the most convenient is the special heart broth with added yeast hydrolysate and swine serum (instead of horse serum) in an atmosphere of carbon dioxide (Fabricant, 1959). Nevertheless, such isolations remain difficult and uncertain, especially when secondary microbial invaders exist. Negative results therefore do not conclusively prove that *M. gallisepticum* is absent.

For this reason serological methods afford a valuable aid in the diagnosis of chronic respiratory disease due to *M. gallisepticum*, e.g. the agglutination test (Adler & Yamamoto, 1956) and the haemagglutination inhibition test (Crawley & Fahey, 1957) provided that the infection in the fowl is caused by a P.P.L.O. of the same serotype as that used as antigen, and that the concentration of antibodies is sufficiently high.

At present our experience indicates that chronic respiratory disease in France is due only to Adler's "S.6" type P.P.L.O.

(2) *Specific bacteria.* All workers who have studied chronic respiratory disease acknowledge the importance of the secondary flora, among which are prevalent *Haemophilus gallinarum* and/or *Escherichia coli*. In France, only *E. coli* is of importance. This supports Nelson's view (1939) of mixed infections by a bacterial species and P.P.L.O. The role of *E. coli* is doubtful since it is an ubiquitous species, including many types and strains, some pathogenic and some not. In the author's laboratory, only one strain out of more than a hundred isolated from cases of chronic respiratory disease has been proved pathogenic; this belonged to the O.119 group (Mollard, 1960). On the other hand, Renault, Guillon & Palisse (1960) found 24 out of 74 strains causing fibrinous lesions in the pericardium and the air sac after intraperitoneal injection of doses of from 100,000 to 1,000,000 organisms. Fifteen of these strains killed the infected chickens in from two to six days' time. Some workers wonder whether one has to distinguish a special respiratory coli infection in which mycoplasmas are not involved from chronic respiratory disease due to a P.P.L.O.

It is too early to give a systematic classification of colibacillary chronic respiratory disease since positive information is still lacking. On the other hand, if the constancy of serological P.P.L.O. reactions is considered, it appears that for the present *M. gallisepticum* should be considered as the primary agent of chronic respiratory disease, and *E. coli* as a secondary invader capable of modifying the clinical aspects and inducing special lesions, typical of which is the caseous exudate in such organs as the air sacs and pericardium.

Special attention must be paid to the "L" forms of bacteria. In 1935, Klieneberger discovered, among the usual colonies in cultures of *Streptobacillis moniliformis*, small colonies composed of ordinary microbial bodies and small organisms looking like P.P.L.O's. The latter could be isolated and kept in cultures in stable form. It was thought that they were really P.P.L.O.'s living as symbionts with the bacteria. Dienes (1939) demonstrated that they represented a variant or evolutive phase of *S. moniliformis*, and his view has been universally accepted. This phase was first described under the initials "L.I." (i.e. Lister Institute), then as "L" only. Since 1939, the phenomenon has been observed with different bacteria, either by spontaneous transformation or under certain experimental conditions such as cultivation in media containing growth inhibitors such as penicillin. Some workers, e.g. McKay & Taylor (1954), Kelton & Gentry (1957), Smith, Peoples & Morton (1957) and Gentry (1960) speculate as to whether the P.P.L.O.'s found in chronic respiratory disease, or at least some of them, could not be "L" forms of *Haemophilus gallinarum*. They claim to have obtained "L" forms with cultures of the above bacillus, whose pleomorphism is well known, using either media containing a heat-killed extract of *H. gallinarum* or deoxyribonucleic acid from *H. gallinarum*, and by alternating with passages in embryonated eggs.

McKay & Truscott (1960) suggest that infectious coryza and chronic respiratory disease might be two aspects of the same disease, the former being

an acute disease due to the bacterial form of *H. gallinarum* and the latter a chronic one due to the "L" form.

Adler (1960) does not accept this view and emphasizes that the "L" form colonies are larger and thicker than the P.P.L.O. ones, that they have irregular and rather coarse surfaces in contrast to the smooth, round, clear *Mycoplasma* colonies and that serial passages of P.P.L.O.'s from broth to agar do not alter colony morphology, whereas the "L" forms of bacteria are very unstable in broth culture, which either stops their growth or causes them to revert to the parental bacteria.

Gentry (1960) admits that *M. gallisepticum* is a P.P.L.O., that it is the chronic respiratory disease agent and that it never reverts to a bacterial form. Moreover he considers that the so-called "non-pathogenic P.P.L.O.s" are quite different, that they cannot be classed as P.P.L.O's and therefore are of bacterial nature. He concludes that if chronic respiratory disease is primarily caused by *M. gallisepticum*, the clinical aspect of the disease can be changed and aggravated by bacteria, or by "L" forms, with which the so-called non-pathogenic P.P.L.O's have to be included.

Chu (1959) considers that there are at present no satisfactory criteria with which to define with certainty all known P.P.L.O's as a special group and to distinguish some P.P.L.O's from "L" bacteria when the latter have been obtained in stable form. He states that the non-pathogenic P.P.L.O's (*M. gallinarum*) are quite capable, as secondary bacterial invaders, of modifying the course of chronic respiratory disease.

(3) *Stress factors*. It is well known that chronic respiratory disease affects only birds which have been submitted to a stress factor. The irregular transmission of M. *gallisepticum* through eggs, and from infected animals to healthy ones, is not sufficient to explain the occurrence of many outbreaks and the recurrence of cases in flocks. The lowered resistance of birds can be due to a virus infection, parasitism, transportation, faulty management, bad hygiene, changes in feeding, etc. A striking example is that of a poultry farm where only the chemically caponized birds developed chronic respiratory disease, whilst the others did not. Brion, Fontaine and Fontaine (1960) analysed the outbreaks of chronic respiratory disease in 60 infected flocks and found 15 with parasitism, 10 with bad hygiene, 5 which had received Newcastle disease vaccine, 5 with infectious bronchitis, 2 with fowl pox, 1 with Newcastle disease and 2 with faulty management. Twenty cases were of unknown status as far as stress factors were concerned.

In the United States it is generally considered that chronic respiratory disease is a disease of overcrowding or bad ventilation or that it is associated with vaccination. For this reason Newcastle disease and infectious bronchitis vaccines, given as a spray or in the drinking water, have to be administered in conjunction with an antibiotic, low calcium diet, so that the mycoplasmas present in the host are inhibited, instead of exerting their virulence during the vaccinal stress.

CONCLUSIONS

(1) Chronic respiratory disease is due to an infection of the respiratory tract by a pathogenic P.P.L.O. which, on morphological, cultural and antigenic characters, can be included in the family Mycoplasmataceae, as the species *Mycoplasma gallisepticum*. The organism corresponds to Nelson's coccobacillary bodies and also causes infectious sinusitis in turkeys. It may be that the above species will have to be divided into several serotypes.

(2) It is suggested that diseases caused by this pathogenic agent, and hitherto known as chronic respiratory disease of fowls and infectious sinusitis of turkeys, be called "Mycoplasmosis" and that the former should be referred to as "fowl mycoplasmosis" and the latter "turkey mycoplasmosis".

(3) The course, mortality, nature and importance of the lesions can be modified by various bacteria such as *Haemophilus gallinarum*, and particularly by *Escherichia coli*, in bacterial or "L" phases, or by non-pathogenic mycoplasmas classified as *M. gallinarum*. Further studies are necessary to decide whether the latter species should remain as mycoplasma or be considered as an "L" phase of a bacterium.

(4) The susceptibility of the fowl is induced or increased by stress factors such as parasitism, natural or vaccinal viral infection, bad management, etc.

A PROPOSED PLAN FOR THE CONTROL OF CHRONIC RESPIRATORY DISEASE

Two aspects are discussed: (I) protection of infection-free flocks and (II) eradication of chronic respiratory disease from infected farms.

I. *Protection of infection-free flocks*

This includes both the protection of individual flocks locally and also the conditions required to prevent the spread of infection to new areas and to ensure good sanitary conditions in both healthy flocks and flocks freed from infection.

Protection of individual flocks

Methods will vary according to the type of husbandry involved.

(a) *Broiler flocks.* (i) The brooding of a great number of chickens on the same premises is undesirable. The flocks should be divided into separate groups which must be kept isolated in order to prevent the dissemination throughout the farm of an infection started in any one pen. In chronic respiratory disease, the hazards presented by the dissemination of dust, excrement and detritus must be borne in mind. Disposition of the pens and/or laying cages and the ventilation system must be designed to minimize these risks.

(ii) The introduction of only infection-free chicks is difficult to achieve. The broiler grower must pay great attention to the choice of his supplier and all newly purchased chicks must be considered as suspect. Consequently their growth, weakness or abnormal mortality (especially about the 20th day of age) must be carefully watched. Autopsy of dead chicks should be carried out and, with the agreement of the chick-supplier, examination of the sera from the

laying stock can be carried out for diagnostic confirmation. Since broilers are not retained for reproduction, treatment with antibiotics might be of some use, since it limits the further spread of infection. However one must recognize that the microbial sterilization of the infected subjects is impossible. Streptomycin and the tetracyclines seem to be the most efficient antibiotics, but it is impracticable on economic grounds to add them to all rations. Perek & Perk (1958) propose the atomizing of streptomycin solution with an aerosol apparatus when the chicks are one day old and again at three or four weeks old. Another efficient method is to give tetracyclines in a low calcium ration for a period of four or five days during the critical periods just after hatching and during the fourth, fifth or sixth week of life (Price & Hare, 1959).

(b) *Breeding flocks.* (i) The flock should be divided into small groups, whilst isolation must also be maintained between layers and their progeny. As far as possible, it is necessary to have separate incubators so that contact is avoided between eggs or chicks coming from the different groups of laying birds. This separation is essential should it prove necessary to detect parent hens in the event of infection occurring among the offspring. Attention should be given to persistent falls in production, to abnormal embryonic mortality on the ninth day of incubation or thereabouts, and to any increasing number of pipped eggs. Diagnostic laboratories can help to detect the infected group of hens by cultivating the mycoplasmas from dead embryos and "pipped" eggs.

(ii) Birds to be kept for reproduction should undergo a serological examination at the ages of two and four months and infected birds should be eliminated.

(iii) Freshly introduced breeding stock must be placed in quarantine. If they are adults, they should have a serological examination when they arrive, and again a month later. If they are chicks, they should be isolated for two months, fed without antibiotics and examined serologically at one month and again at two months of age.

In all cases it is advisable to keep a record of all purchases so that if necessary the source of all birds can be traced.

General measures of protection

Three points must be considered:

(1) *Control of importations.* Under French regulations eggs and live fowls from foreign countries can be imported only under licence, and it is required that the flock of origin is under veterinary supervision. Unfortunately, poultry farmers do not always appreciate that their own and the industry's interests depend on the observation of this regulation and too many farmers illegally import stock. Severe penalties should be imposed if the order is not observed.

(2) *Control of breeding flocks.* At the present time, control measures deal only with pullorum disease. Many infected flocks spread chronic respiratory disease by the distribution of chicks and hatching eggs. Purchasers have no guarantee of freedom from infection and generally have no idea of the risks incurred. They have difficulty in obtaining compensation since, owing to the long incubation period and the slow development of symptoms, it is rarely possible to prove that infection was present prior to the sale. A good policy would be

to prohibit the sale of hatching eggs and day-old chicks except by farms holding a certificate of freedom from infection. To qualify for this certificate the poultry farmer would have to agree to carry out the following conditions:

(a) To keep a record of the causes of mortality or "culling" of all adult birds together with the production figures, percentage fertility, deaths in shells, number of eggs hatched and losses after hatching. These records would be of value to the veterinary officer tracing outbreaks of chronic respiratory disease.

(b) To carry out serological examinations on all birds newly introduced into the flock.

(c) To carry out two consecutive serological examinations at an interval of a fortnight on one-tenth of each group in turn within a six-month period in order to control the whole flock.

The diagnosis of the presence of chronic respiratory disease would result in the withdrawal of the certificate for the following year, the certificate to be re-issued only after proof that the infection had been eradicated. Breeding farms within this plan must not sell hatching eggs or chicks from other sources, under penalty of one year's removal of the certificate.

(3) *Control of live egg-propagated vaccines.* Live vaccines obtained from egg-culture may carry mycoplasmas; the control of these vaccines by their cultivation on appropriate media for P.P.L.O's should be compulsory, and the label should state that the vaccine sold or to be sold is free of any avian mycoplasma.

II. *Eradication of chronic respiratory disease in infected farms*

(a) *Broiler flocks.* The following measures must be applied: The infected groups must be strictly isolated until slaughter, and treated with antibiotics. After depopulation the premises must be carefully disinfected. Restocking should be made with chicks from uninfected flocks and the new groups may be systematically treated with antibiotics during the critical periods, as indicated in I (a) (ii).

(b) *Breeding flocks.* Careful records of sales will indicate the flocks which might have been infected and which require sanitary supervision in order to prevent recurrence of the disease: As soon as a diagnosis is made, the supply of eggs or chicks for restocking should be discontinued. The best method is certainly to slaughter the infected groups although they may be retained temporarily to produce table eggs.

These radical measures often meet with opposition for economic reasons. If they were made compulsory they would either cause bankruptcy or would be disregarded and outbreaks would remain unreported. It seems preferable therefore to leave it to the farmer himself to apply less stringent measures with the help of his veterinary surgeon, although it would be understood that any health certificate would be compulsorily withdrawn during the period of eradication.

It is recommended that during this transitory period of eradication efforts should be made to obtain uninfected eggs from infected hens by the following method. Breeding hens which have been injected parenterally with 50 to

200 mg. of streptomycin or a tetracycline will lay eggs uninfected with mycoplasmas (or at least a minimal number of infected eggs) during the subsequent four to eight weeks. Consequently, one such injection per month should be made. Before incubation, the eggs should be disinfected with formalin or a quaternary ammonium compound against microbial infections, and then soaked in a dip of antibiotic (erythromycin or tetracycline) which will penetrate the shell and by its subsequent spread to the albumin and yolk destroy mycoplasmas without affecting the embryo. The hatched chicks should be exposed to formaldehyde gas or to a streptomycin aerosol and brooded in separate groups. A serological examination should be made of all chickens hatched under these conditions at two, four and six months old. Food should not contain antibiotics. This is one method of rebuilding an infected flock, the infected breeders then being killed at little economic loss.

CONCLUSIONS

The eradication of chronic respiratory disease is an important problem for the poultry industry and a plan is proposed for the protection of healthy flocks and the elimination of infection from affected farms by means of local, general and even international measures. This may be carried out by the application of serological methods for the detection of chronic respiratory disease, the slaughtering of infected flocks and restocking with birds raised on uninfected premises.

SUMMARY

The aetiology, symptomatology, pathogenesis and differential diagnosis of chronic respiratory disease in chickens are discussed. It is suggested that the terms "chronic respiratory disease" and "turkey sinusitis" be replaced by "mycoplasmosis" and "turkey mycoplasmosis".

Detailed recommendations for the eradication of mycoplasmal infection in broilers and breeding flocks are described. A plan is outlined for the control of the disease on a national scale by the issue of health licences to non-infected flocks, supported by legislative measures.

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RESPIRATORY DISEASE COMPLEX OF CHICKENS IN THE UNITED STATES*

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Today, as in the past, the poultry industry in the United States is confronted with a serious disease condition that is of considerable economic importance to the poultryman. The mystery and apparent complexity of the respiratory diseases today does not materially differ from the confusion that existed in the twenties. At that time it was not known that vitamin A deficiency, infectious coryza, fowl cholera, and diphtheritic fowl pox were separate disease entities. The confusion existed when two or more of these diseases occurred in a flock at the same time. Once this complex condition was recognized and effective means of diagnosis for each disease were made available, measures for prevention and control soon followed.

AIR SAC INFECTION

Soon after World War II the condition referred to as "air sac disease" or "chronic respiratory disease" became familiar by both terms among poultry pathologists and poultrymen alike. By 1951, the incidence of the disease had so increased as to threaten the broiler industry along the eastern seaboard of the United States. During 1952, a delegation from that area conferred with Dr. B. T. Simms and his staff, of the United States Bureau of Animal Industry, at a meeting which included pathologists representing all parts of the nation (Anon., 1952). It is interesting to note that observations made at experimental stations suggested that the condition was not a specific infection or disease process, but a disease associated with many agents, including *Mycoplasma gallisepticum*, which is the cause of the specific infection known as chronic respiratory disease.

In addition, a critical survey was conducted by the veterinarians to study the disease in poultry flocks under field conditions. It became quite evident that measures of sanitation in these areas were at an extremely low point of maintenance. There was no control of visitors on the premises, and sanitary precautions against introduction of disease were neglected and practically non-existent. It was also observed that other respiratory diseases of poultry were present where air-sac infections existed. Complicating or precipitating factors in air-sac infection appeared to be actual field outbreaks of infectious

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† Methods for isolation of mycoplasmas and other agents were unkown at this time and were therefore not conducted.

bronchitis, Newcastle disease, and laryngotracheitis or the use of live virus vaccines against those diseases.

FACTORS CONTRIBUTING TO THE COMPLEX

All of us have asked ourselves the same question, "What is the reason for the sudden increase and widespread occurrence of respiratory diseases of poultry?" The answer to this question cannot be given without considering changes in poultry husbandry practices, including methods at present prescribed for the prevention and control of diseases.

During the past two decades not only have numbers of birds increased, but also birds per farm. Other contributing factors are multiple brooding and concentration of poultry within areas. To these circumstances should be added:

(1) Use of live virulent virus (potentially disease-producing) vaccines (against laryngotracheitis, Newcastle disease, infectious bronchitis and fowl pox).

(2) The highly contagious nature of the causative agents, spreading easily from bird to bird and area to area.

(3) Transmissibility of some of these agents through hatching eggs. Under these circumstances, it is not difficult to understand the reasons for today's involved respiratory disease complex.

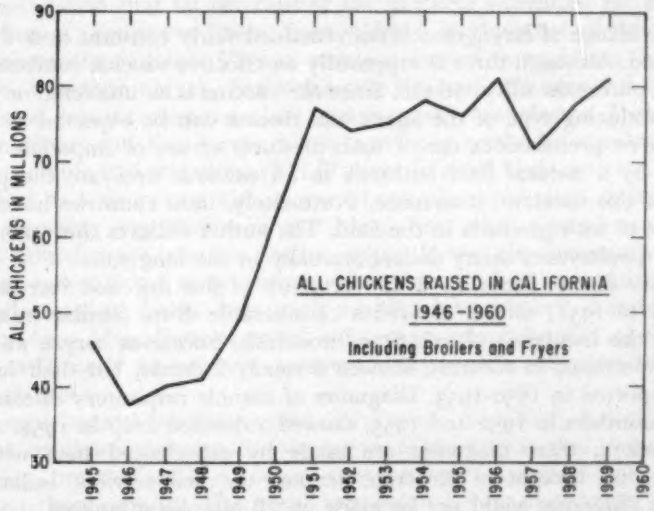

Fig. 1. Chicken population in California, 1949–1960, including broilers and fryers.

Fig. 1 illustrates the marked increase in the number of chickens raised in California since 1946. This sharp increase was characteristic of all parts of the United States. The value of the poultry industry rose from half a billion

dollars in 1938 to 4½ billion in 1955 (a ninefold increase in 17 years). During this period of rapid expansion in California an equally phenomenal rise in respiratory diseases was also experienced, accompanied by confusion in diagnosis.

Incidence and types of respiratory diseases. Table I presents the incidence of respiratory diseases diagnosed between 1946 and 1954 in the southern part of California by a state diagnostic laboratory. *These figures should not be taken as absolute but should serve only as a guide to the trend taken by the various conditions diagnosed by experienced veterinary pathologists during this period in a poultry area.*

TABLE I

INCIDENCE OF RESPIRATORY DISEASES DIAGNOSED BY THE CALIFORNIA STATE PATHOLOGICAL LABORATORIES DURING THE PERIOD OF 1946 THROUGH 1954

Disease	*Number of cases during year*								
	1946	1947	1948	1949	1950	1951	1952	1953	1954
Newcastle disease	267	417	718	752	867	1005	712	690	458
Infectious bronchitis	61	75	146	311	335	520	505	612	99
Coryza and colds	445	569	880	1440	760	1013	909	953	871
Laryngotracheitis	210	290	225	309	236	287	290	290	288
Air sacculitis	11	157	186	329	—	—	—	—	905
Chronic respiratory disease	—	—	—	—	—	—	1426	2694	172

The incidence of laryngotracheitis remained fairly constant over the nine-year period. Although there is supposedly an effective vaccine combatting this infection, outbreaks still continue. Since the vaccine is an unaltered or virulent disease-producing type of the agent, this disease can be expected to prevail. Improper or promiscuous use of such products or use of impotent vaccines followed by a natural field outbreak in an enzootic area are the probable causes for this constant occurrence. Fortunately, most countries have control of the use of such products in the field. The author believes that such control will save poultrymen many dollars annually in the long run.

Newcastle disease. From 1946 the incidence of this infection increased progressively to 1951; then it showed a considerable drop. Similar trends were noted in the incidence of infectious bronchitis, infectious coryza and colds. Air-sac infections, in contrast, showed a steady increase, but their incidence was unreported in 1950-1953. Diagnoses of chronic respiratory disease, made in large numbers in 1952 and 1953, showed a decided drop in 1954. As mentioned before, these diagnoses are made by experienced men with good facilities, but, because of the large demand on their services, isolation and definitive diagnoses could not be made on all samples submitted.

It is interesting to note, however, that chronic respiratory disease was conspicuous by its absence in 1947-1951. There is no doubt that some of the cases diagnosed as coryza and colds during those years were due either to the chronic respiratory disease agent alone, or were a combination of chronic respiratory disease and some other respiratory disease. Under field conditions,

infectious coryza, chronic respiratory disease, and a mixed chronic respiratory disease infection are similar and can be easily misdiagnosed. Special and elaborate laboratory procedures are necessary to detect and distinguish between them.

It is interesting to note a sharp rise in the incidence of coryza and colds (chronic respiratory disease?), air-sac infection, and Newcastle disease, beginning in 1949. That was a year when the mild (B1 strain) live virus vaccines were introduced to the poultry industry as immunizing agents against Newcastle disease. Vaccination of chickens by the respiratory route (intranasal) began in 1950. Again, a sharp increase in the diagnoses of not only Newcastle disease but also coryza and colds was found in 1951. These sudden increases were not due only to the increase in poultry populations, but may very well be correlated with the widespread use of live viral vaccines.

EVIDENCE OF MULTIPLE AETIOLOGY IN RESPIRATORY DISEASES

Severe and complicated infections of the respiratory system, including air sacculitis, were noted in California as early as 1946. On a number of occasions, examination of young chickens with severe caseous air sacculitis yielded Newcastle disease virus to the exclusion of other known agents†. During 1952-1953, an intensive survey was conducted at the experimental station of the University of California to determine the aetiological factors involved in chronic respiratory disease conditions encountered in the field (Anon, 1953) It was soon found that 60 per cent of the chickens submitted for diagnosis suffered from a respiratory disease from which a combination of two or more agents was readily isolated. Various combinations of mycoplasma, infectious bronchitis, infectious coryza, *Escherichia coli*, Newcastle disease and fowl pox were isolated, but the most prevalent organism was mycoplasma. Fortunately, Adler, Fabricant and Yamamoto (1958) developed methods for culturing the pleuropneumonia-like organisms (PPLO) from infected birds, and the method was applied as a diagnostic aid. A second test, the rapid slide agglutination test for detecting agglutinins in the blood, was also applied as a rapid means of detecting the infection (Adler, 1954). It was also demonstrated that some viral agents acted as synergists, enhancing existing mycoplasma infections (Adler, 1955). Laboratory trials readily demonstrated that infectious bronchitis virus (Massachusetts strain) enhanced a relatively mild mycoplasma infection sufficiently to produce a severe disease with extension of lesions into the air sacs.

In an experimental laboratory trial (Bankowski, unpublished data), inoculation of mycoplasma cultures into the sinuses of chickens caused no symptoms or mortality, but resulted in a 100 per cent serological response that persisted for at least three months. The agent was isolated from the sinuses 60 days after inoculation, but was not recovered 30 or 90 days after. When *E. coli* was inoculated in conjunction with the mycoplasma, mortality was 45 per cent within five days. A fibrinous pericarditis and perihepatitis was found in all of the birds that died, and *E. coli* was readily isolated. Twenty-four days later 72 per cent of the surviving birds were serologically positive for myco-

plasma, and three months later all six surviving birds presented serum agglutinins. Birds from these groups killed in the first, second, and third month did not yield the mycoplasma upon culture on the first or third month, but 22 per cent yielded positive cultures 60 days after inoculation. *E. coli* was not recovered from the survivors. Among a group of birds given *E. coli* alone, the bacterium was easily isolated from the sinuses and tissues of birds that died soon after inoculation, but not from birds which were sacrificed 30, 60 or 90 days after inoculation. These results suggest that *E. coli* is a self-limiting opportunist and that a serious disease resulting in mortalities can be expected from a combination of *E. coli* and other relatively mild agents such as mycoplasmas.

To demonstrate that viral agents used in vaccination can cause a serious respiratory infection when administered in combination, a flock of 3,500 three-week-old chickens, obtained as day-old chicks from a commercial hatchery, were given a combination of infectious bronchitis and Newcastle disease vaccines by the spray method under field conditions (Fig. 2) (Bankowski, Raggi & Hill, unpublished data). Admittedly, the vaccination was conducted on an unusually cool and rainy late afternoon, which was considered a stress factor. In addition, the chicks had received "Coxine" at three days of age. A severe respiratory reaction occurred, characterized by a severe tracheitis, caseous plugs in the trachea, and a mortality of 3·6 per cent during the ensuing two-week period. Similar results with a mortality of 4·6 per cent were obtained in a second replacement flock exposed to the same treatment on the same day. Both infectious bronchitis and Newcastle disease viruses were readily isolated from the tracheal exudate, but neither mycoplasma nor coliforms were demonstrated. On necropsy typical air-sac involvement was observed. In a trial with two-week-old chickens an air sacculitis, pericarditis, and perihepatitis resulted from the same combination of vaccines administered in the drinking water. The chicks had received "Coxine" at three days of age. *E. coli* was isolated from the exudates on the affected organs; however, no PPLO or agglutinins were demonstrated in the blood sera (Fig. 3).

It is obvious from these trials that serious chronic respiratory diseases of poultry are associated with, or are caused by, a plurality of agents of varying pathogenic potential. The most extensive studies of the chronic respiratory disease complex of poultry flocks under field conditions were by Van Roekel, Gray, Shipkowitz, Clarke and Luchini (1957), and Sullivan, Gill, Somer and Heddleston (1957). Those workers concluded that mild respiratory infections such as chronic respiratory diseases may be precipitated or aggravated by viruses, introduced either through vaccination or natural infection, and that a number of aetiological agents can influence the course of a milder respiratory infection.

In none of these instances has a basic and fundamental approach been made towards elucidating the *modus operandi* of the respiratory condition involving the air sacs of poultry that may account for the high rate of condemnation, nor have the more recently isolated agents of low virulence been evaluated in this serious entity.

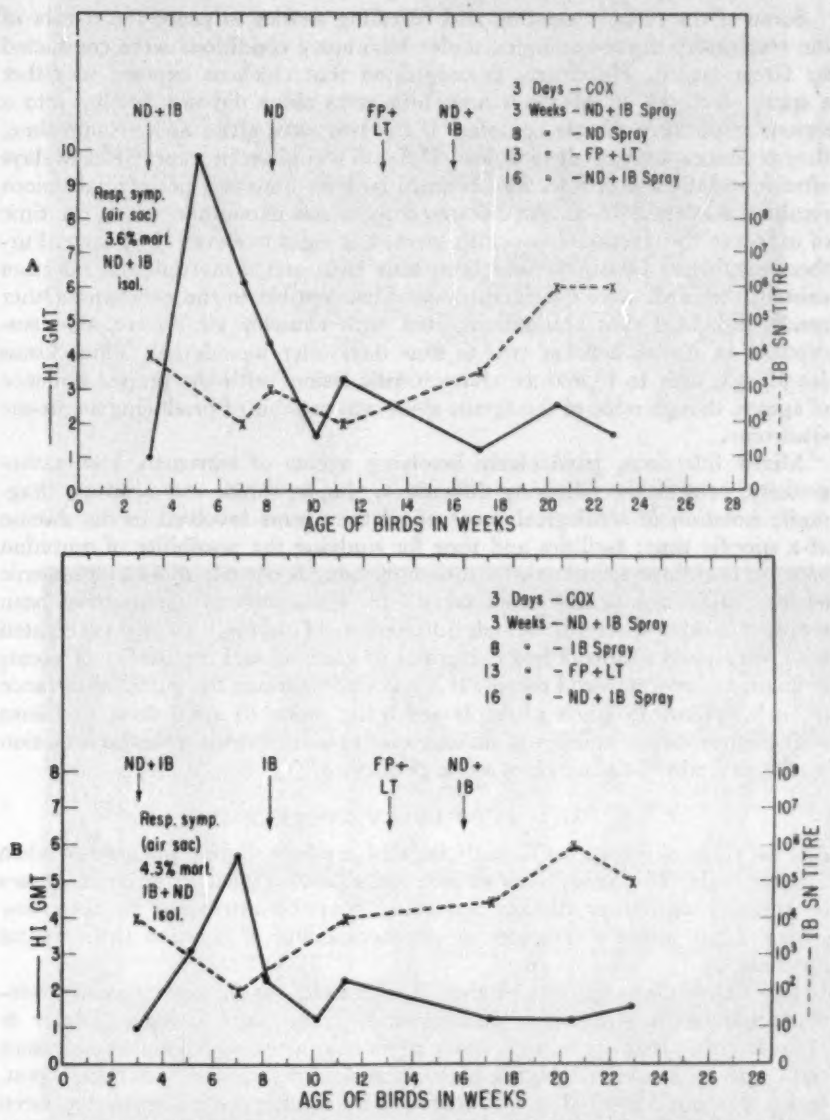

Fig. 2. Serological response in chickens of two replacement flocks (A and B) that suffered a respiratory infection after a combination of Newcastle disease (ND) and infectious bronchitis (IB) vaccine given by the spray method.

FP+ LT —Laryngotracheitis.

Data from series of field trials using commercial vaccines (Bankowski, Raggi and Hill, unpublished data).

Some of the most interesting and revealing studies to prove the nature of the respiratory disease complex under laboratory conditions were conducted by Gross (1958). He clearly demonstrated that chickens exposed to either a spray of *E. coli* or infectious bronchitis virus alone did not develop into a serious respiratory disease complex. If the two were given at the same time, they produced a slight air sacculitis. If *E. coli* was given in a spray eleven days after inoculation with infectious bronchitis virus, however, pericardial lesions resulted. Susceptibility to the disease complex was maximum, not at the time of exposure to infectious bronchitis virus, but eight to eleven days later. Furthermore, when both infectious bronchitis virus and a mycoplasma infection existed, the birds were considerably more susceptible to the coliforms. Other results indicated that chickens infected with Crawley virus were most susceptible to *E. coli* aerosols two to four days after inoculation. Thus, Gross (1958) was able to reproduce characteristic lesions with the proper sequence of agents, though none of the agents alone was capable of producing an air-sac syndrome.

Mixed infections, particularly involving agents of extremely low pathogenicity, present the following difficulties: simple, rapid, and accurate diagnosis; isolation or serological proof of all the agents involved in the disease at a specific time; facilities and time for studying the possibility of mutation of more fastidious agents; and a source of animals entirely free of pathogenic or interfering agents. Infections caused by a plurality of agents have been reported in other species of animals (interference of immunity in hogs vaccinated with attenuated strains of hog cholera virus vaccine, and a plurality of agents in pneumonias of pigs and sheep). It is unsound to attach too much importance to such similarities when attempts are being made to solve these problems with poultry, but a number of investigations point towards a similar situation in the respiratory disease complex of poultry.

AGENTS OF LOW VIRULENCE

At least three of the agents recently isolated are only slightly pathogenic when present singly. The infrequency of their identification during routine diagnoses in chronic respiratory disease conditions may be attributed to their low pathogenicity and the difficulty or impracticability of isolation with present methods.

The Fahey-Crawley virus (Fahey & Crawley, 1954), more recently reinvestigated by Subramanyam and Pomeroy (1960) and Hanson, Filmer & Quiroz (1960), is a very minute, stable agent causing extremely mild respiratory signs and characterized by its poor immunogenicity. The C.E.L.O. agent, which has not attracted much attention by poultry pathologists, has been demonstrated by Sharpless and Jungherr (1960) to exist as a commensal in apparently normal chickens.

The author and his colleagues (Bankowski, Corstvet & Clark, 1960; Bankowski and Corstvet, 1961) isolated an avirulent agent from the respiratory tract of chickens suffering from an unusually severe outbreak of laryngotracheitis. A practising veterinarian had described what appeared to be an outbreak

Fig. 3. Pericarditis and perihepatitis folowing vaccination with combination of Newcastle disease and infectious bronchitis viruses by the drinking water methods to a flock of two-week old chickens.

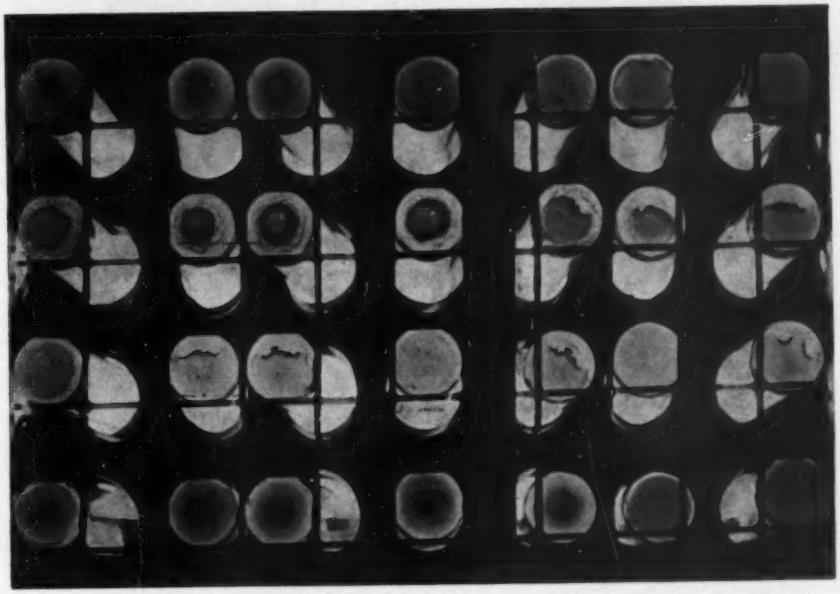

Fig. 4 Haemagglutination inhibition test using Newcastle disease virus and the respiratory disease agent with sera of chickens recovered from both infections.

Rows 1 and 2: Using 4 units of Newcastle disease virus with anti-Newcastle disease (Row 1) and anti-respiratory disease agent sera (Row 2).

Rows 3 and 4: Using 4 units of respiratory disease agent with chicken anti-Newcastle disease (Row 3) and anti-respiratory disease agent sera (Row 4).

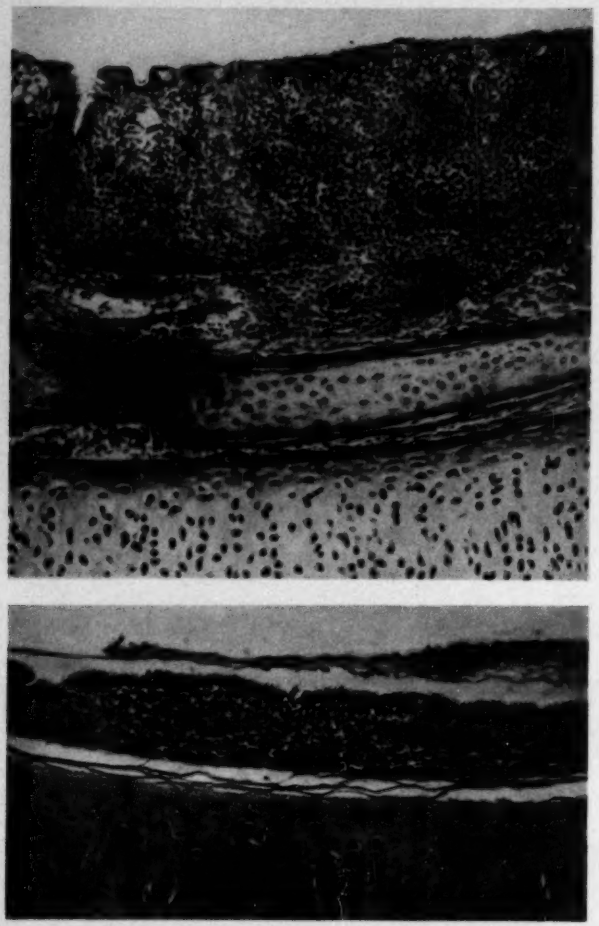

Fig. 5. Lymphoid infiltration of lamina propria of tracheas of chickens inoculated with the respiratory disease agent 6 (top) and 14 (bottom) days previously.

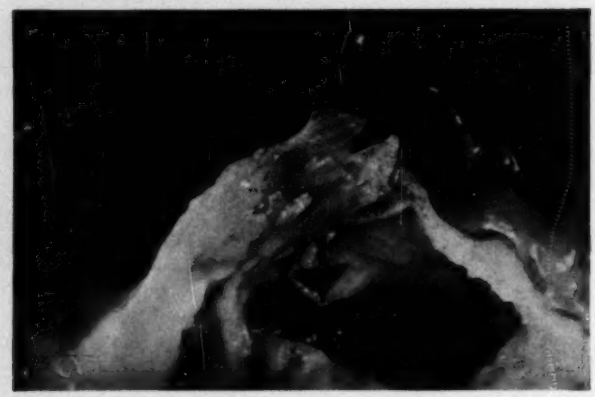

Fig. 6. Air sacculitis produced in uninoculated susceptible six-week-old caged chickens held in a room containing birds infected with the respiratory disease agent and other poultry pathogens.

of laryngotracheitis, but was puzzled by a mortality of over 20 per cent in the group of broilers in 24 hours and an unusually rapid spread of the infection to other pens on the premises. Examination of the tracheas revealed moderate congestion, with petechial haemorrhages in the mucosa and considerable caseous exudate in the larynx and lumen in the upper-third of the trachea. Laboratory procedures revealed in the allantoic fluids of embryos inoculated with the exudates an agent that haemagglutinated chicken red blood cells, but could not be separated from the mixture with a known hyperimmune chicken anti-Newcastle disease serum. It was soon learned that the agent was immunologically and serologically distinct from other known avian viruses and agents of the myxo-virus group. By itself, the respiratory disease agent caused mild respiratory signs in some, but not all, of the birds inoculated intratracheally, but was capable of producing a haemagglutination inhibition antibody that specifically inhibited haemagglutination in a homologous system. By this means it could be readily separated from Newcastle disease. Fig. 4 illustrates the haemagglutination inhibition test, with Newcastle disease virus and the respiratory disease agent being used with sera of chickens which had recovered from both infections. The agent is readily propagated in tissue cultures of HeLa and swine kidney cells and in chicken embryonating eggs inoculated into the allantoic sac or the chorioallantoic membrane.

Intratracheal inoculation of infected allantoic fluids of chicken embryos produced mild, moist, audible rales between the fourth and the sixth days. The virus can be readily isolated from the tracheas of infected chickens on the fourth day. Fig. 5 illustrates the lymphoid infiltration of the lamina propria of tracheas of chickens infected six and fourteen days previously with the respiratory disease agent.

Although this agent alone does not produce a serious clinical respiratory infection, it was found to spread from infected to susceptible chickens in the same room, and, when it was found in combination with other agents, e.g., Newcastle disease, *Haemophilus gallinarum*, infectious bronchitis and mycoplasma, a severe and chronic respiratory disease condition with air-sac involvement developed in susceptible uninoculated chickens held in the same environment (Fig. 6). At the present time, studies relative to the role of the avirulent respiratory disease agent in the chronic respiratory disease complex are in progress. Particular attention is given to sequence and time of exposure based upon observations made by Jungherr, Chomiak & Luginbuhl (1957), and Gross (1958). These authors associated the optimum period of susceptibility to chronic infection due to a multiple aetiology to be when the superimposed infection is introduced at the time of the strongest lymphoid reaction to the initial infection.

The discovery and the importance of the more recently isolated agents do not necessarily indicate that they are the underlying cause for the present respiratory disease complex, but strongly point to a possibility that their presence with other viruses or bacteria may also precipitate a chronic and serious respiratory disease infection. Because of the seriousness and apparent increase in severity of respiratory diseases in poultry flocks, the role of these

and perhaps other agents of lower virulence must be determined and evaluated in respiratory infections of mixed aetiology before the problem can be elucidated.

SUMMARY

Infections of the respiratory tract of chickens characterized by chronic and severe lesions of the nasal passages, sinuses, tracheas and air sacs are a major problem in the U.S.A. There appears to be a marked correlation in their incidence with:

(1) The expansion of the broiler industry and increase in poultry populations;

(2) Changes in husbandry, multiple brooding, increases in population density, and deterioration in sanitation and disease-control measures;

(3) Introduction of mass methods of vaccination administered chiefly by the respiratory route and using live virulent and contagious agents (Newcastle disease and infectious bronchitis).

A review of the literature indicates that chronic respiratory diseases of poultry are caused by a plurality of agents of varying pathogenic potential. Relatively mild respiratory infections may be precipitated or aggravated by vaccination or natural exposure to agents known to be pathogenic to chickens (*Mycoplasma*, *Haemophilus gallinarum*, *Escherichia coli*, infectious bronchitis Newcastle disease, laryngotracheitis and fowl pox).

One survey showed that 60 per cent of respiratory diseases yielded two or more of the above pathogenic infectious agents, *Mycoplamsa* being by far the most prevalent. Viral agents may act as synergists that enhance existing mycoplasma infections, whilst serious respiratory disease may be produced with combinations of agents exclusive of *Mycoplasma*. Air sacculitis, pericarditis and perihepatitis have been observed after giving a flock of two-week-old chicks a combination of infectious bronchitis and Newcastle disease vaccines in the drinking water; besides the viruses, *E. coli* was also isolated, but not *Mycoplasma*.

Recent work has shown that maximum susceptibility of chickens to *E. coli* occurred 8-11 days after exposure to a virulent poultry virus, whilst if both infectious bronchitis and mycoplasma infections existed the birds were more susceptible to *E. coli*. None of the agents alone was capable of producing an air-sac syndrome.

At least three new agents of low pathogenicity have been isolated recently and although they are not necessarily the underlying causes of the respiratory disease complex, there is a strong possibility that their presence with other agents may precipitate chronic respiratory infection.

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A PROPOSED CLASSIFICATION OF THE LEUCOSIS COMPLEX AND FOWL PARALYSIS

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When Ellerman (1920) introduced the term leucosis to designate a neoplastic condition of fowls which affects haematopoietic tissue, he was in fact stressing a difference between the human leukaemias and analogous conditions in fowls. Whereas leukaemia, as defined by Virchow (1845), meant literally "white blood", implying not only anaemia but the presence of large numbers of immature leucocytes in the circulating blood, the condition in fowls, with one notable exception, is not characterized by leukaemia, except perhaps terminally. The common form of leucosis appears as an extravascular infiltration of malignant cells in many different organs, causing great enlargement and death from functional interference. The cells involved are either lymphoblasts, myeloblasts, or erythroblasts in various stages of differentiation ranging from extremely primitive large "stem cells" which cannot be identified, to those which are fairly easily recognizable upon histological examination. It is true to say, as it is for other neoplastic conditions, that the more undifferentiated the cell type involved, the more rapidly growing and malignant the resulting tumour.

Fowl leucoses in one form or another were recognized as far back as 1868 by Roloff. It is not intended to give here a historical survey of the vast literature covering these diseases, as a good account has already been given by Furth (1946) and Panima (1957), to mention but two reviewers. It is sufficient to say that the group of diseases quickly became one of the most serious threats to a rapidly expanding poultry industry, and it has been calculated by Blaxland (1956) that seven to eight million pounds sterling are lost annually in Britain because of the leucotic complex, which in this particular context is taken to include the various types of fowl paralysis. The comparable figure in the U.S.A. in 1955 was about 73 million dollars and now must be nearer 100 million dollars.

Fowl paralysis was included in these estimates and the necessity for its inclusion reflects the present uncertainty regarding this condition and its relationship to the leucoses. Fowl paralysis, initially described by Marek (1907) and called by him "polyneuritis", was first studied intensively by Pappenheimer, Dunn and Cone (1926), who described it as an aleukaemic transmissible disease sometimes associated with ovarian lymphomata and iritis and called it *neurolymphomatosis gallinarum*. The visceral lesions sometimes occurring in neurolymphomatosis were considered by Pappenheimer to be aetiologically related to the neoplastic lymphoid tumours of discrete

lymphoid leucosis (lymphocytoma) and this view received the support of Johnson (1932) and Paterson, Wilke, Murray and Henderson (1932), who could see no essential difference between them.

In 1933 Furth reported the results of transmission experiments with a strain of lymphoid tumour which could also apparently manifest itself as a myeloid or even an endothelioid tumour. This he called lymphomatosis, and he said it was rare compared with neurolymphomatosis and its associated visceral lesions. In this he agreed with Mathews and Walkey (1929) and Feldman and Olson (1933), who, however, failed to transmit the condition. Subsequently Fenstermacher (1936) stated that he was unable to transmit either lymphocytoma or neurolymphomatosis.

CONFUSION OF NOMENCLATURE AND AETIOLOGY

It was at about this time that the confusion which lasts to the present day regarding nomenclature and aetiological relationship became apparent. The situation had arisen where on the one hand lymphoid leucosis or lymphocytoma was related to fowl paralysis, was transmissible and could develop into other forms, whilst on the other it was not transmissible and was unrelated to fowl paralysis. Some workers were using the term "visceral lymphomata" or "lymphomatosis" to mean the lymphoid neoplastic disease, while others meant the visceral tumour-like lesions associated with fowl paralysis, and yet others could see no difference between the two conditions and used the term "visceral lymphomatosis" to cover both conditions.

In 1937 Jungherr indicated, on the basis of transmission experiments from field cases, that he favoured the unitarian view regarding the common aetiology of fowl paralysis in its various manifestations and the lymphomatosis of Furth. However, Lerche and Fritzsche (1934), after a careful comparative study, stated that they considered neurolymphomatosis a misnomer and that the condition should be more accurately called neurogranulomatosis, since the condition had many characteristics of a chronic inflammatory condition. Marek's original identification of the disease as a neuritis thus belatedly received support. Unfortunately Fritzsche's paper did not attract the attention it deserved, especially in the English-speaking world, and the general tendency to classify fowl paralysis with the leucoses persisted, as witness the report of Jungherr, Durant and Lee (1941) in which, although disclaiming any intention of implying a common aetiological basis, they presented a classification of the leucosis complex which included visceral and neural lymphomatosis, ocular lymphomatosis, osteopetrosis, erythroblastosis, granuloblastosis and myelocytomatosis.

Despite their disclaimer, this classification became generally adopted and is now to be found in most textbooks of avian pathology.

However, some workers did not find this classification satisfactory, and Campbell (1945), and Burmester, Prickett and Belding (1946), like Davis, Doyle, Walkey and Cenker (1947) published results which seemed to dissociate fowl paralysis from lymphoid leucosis and the leucotic complex. The confusion regarding nomenclature has been well illustrated by Hungerford (1951),

who published a list of 69 synonyms for the leucotic and possibly allied diseases, covering in all probably not more than six to seven disease entities, not all of which may be in the complex.

A classification has been suggested (Campbell, 1954) which it was hoped would be generally acceptable and would remove much of the current confusion (see Fig. 1). It was maintained that there seemed to be no valid reason why fowl paralysis in all its forms should not be removed from the leucotic complex and also that available evidence gave good grounds for separating osteopetrosis not only from the complex, but from fowl paralysis as well. Support for this has recently been forthcoming from Gross, Burmester and

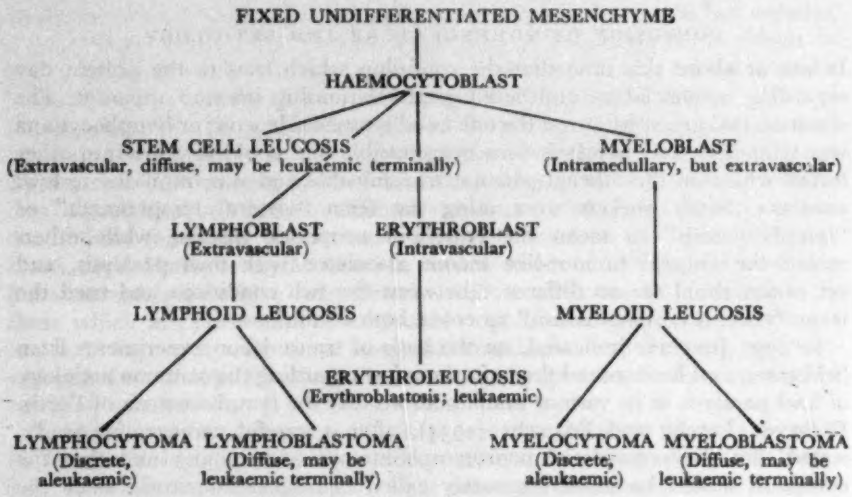

Fig 1. Proposed classification of the leucosis complex.

Walter (1959), who categorically state that they consider the leucoses and fowl paralysis in its various manifestations to be unrelated entities. It would seem, however, that they are not prepared to exclude osteopetrosis, since their recent work (Burmester, Walter, Gross and Fontes, 1959) on the oncogenic spectrum of certain "pure" strains of leucosis showed that a number of cases of osteopetrosis developed in chickens inoculated with Beard's "Strain A" myeloblastosis.

At this juncture it would be useful to survey briefly the pathological conditions involved, as they appear in spontaneous field cases.

Lymphoid leucosis (lymphoblastoma, lymphocytoma or visceral lymphomatosis of some workers).

This is a neoplastic condition affecting cells of lymphoid origin and is essentially

an extravascular disease. The liver is almost invariably the main organ involved, and as it is certainly the most obvious upon post-mortem examination it is a useful organ on which to base a descriptive classification. For example, the liver may not be much enlarged, and may contain numbers of discrete, firm, creamy-white nodules protruding from the surface. Similar tumours may be present in other organs such as kidney, heart, lungs, intestines, bursa of Fabricius, etc. Indeed few organs are exempt. The spleen is initially somewhat enlarged, but may terminally be atrophied. This is the discrete form of lymphoid leucosis, and it passes through an infinite series of gradations with the opposite extreme which may be called the diffuse type, characterized by great enlargement of the liver, which is smooth and ranges in colour from cream to grey streaked with red. Other viscera show a similar appearance. The central and peripheral nervous systems only rarely show primary involvement and the same is true of the bone marrow, although terminal leukaemic cases (which are very uncommon) may show small grey tumours in the marrow.

The ovary, if affected, presents a granular appearance when immature, whilst the mature organ shows a mixture of tumorous pedunculated follicles and normal follicles.

Histologically the cell type usually reflects the category observed at post-mortem examination. That is, the discrete form is associated with fairly well differentiated lymphoid cells showing few mitotic divisions and growing mainly by expansion, whilst the diffuse form has immature lymphoblastic cells which are rapidly dividing and infiltrating the organ between the columns of liver cells and the sinusoidal membrane. All gradations exist, between the two extremes, but they can usually be correlated fairly accurately with the gross characteristics evident at post-mortem examination.

In general it can be stated that all the scattered lymphoid tissue in the body of the fowl, as described by Lucas (1949) and Biggs (1957), is involved in lymphoid leucosis, especially of course in its more malignant forms. The thymus, however, appears to be only rarely affected.

Laboratory studies have shown in the main that lymphoid leucosis, particularly the discrete form, is not easily transmissible by whole-cell inocula, and that a virus, if present, is difficult to demonstrate. Exceptions to this are provided by Olson's visceral lymphomatosis isolated in 1941 and extensively studied over a long period by Burmester and his colleagues as tumour RPL/12. A spontaneous lymphoid leucosis associated with a poorly differentiated cell type has also been successfully transmitted by whole-cell inocula in the flock of the Poultry Research Centre, British Empire Cancer Campaign, at Edinburgh and is currently being studied. Attempts to demonstrate its filterability have so far failed.

Myeloid leucosis

This is a neoplastic disease affecting the cells of the granulocytic series, i.e. the precursor of the eosinophils, basophils and heterophils. In so far as these cells are mainly found in the marrow of adult fowls, myeloid leucosis can be regarded as of intramedullary origin, although the main growth of cells in this

site is extrasinusoidal. However, myeloid metaplasia is of frequent occurrence in birds, especially in the portal-tract region of the liver, and such centres probably also contribute foci of cells susceptible to an oncogenic agent. As with lymphoid leucosis, two extreme forms of myeloid leucosis can be conveniently described. The diffuse form is associated with a greatly enlarged liver and spleen, the former presenting a firm, granular and often dryish appearance. The kidneys are frequently involved and the marrow is invariably affected, being pinkish-grey in colour, and with large numbers of cells. Histologically the cells are seen to be large myeloblasts or premyelocytes, and these may overflow into the circulation shortly before death, to produce a true leukaemia. The discrete form is known as myelocytoma and offers no difficulty in diagnosis. Friable masses of tumour tissue—resembling baker's yeast—occur in the internal aspect of the sternum, along the costal borders and especially at the costochondral junctions. The ovary is usually affected, but is not much enlarged, and the liver frequently shows considerable periportal aggregations of myelocytes. The kidneys are not always affected, but when they are, they may even be found ensheathed in tumour tissue arising apparently from the internal aspect of the pelvic girdle. The cells infiltrating these and other organs are myelocytes with a vesicular chromophobe nucleus and prominent eosinophilic granular cytoplasm. They tend to grow and infiltrate in columns and mutual pressure may give them a cuboidal form. The bone marrow is not so strikingly abnormal as in the diffuse form, but histologically it is mainly composed of myelocytes. There may be a terminal leukaemia.

Erythroleucosis

This condition is exceptional in being a true leukaemia from the outset. The diffusely enlarged cherry-red liver and spleen, occasional petechiation in the musculature, connective tissue and heart, the ascites, the pale, anaemic, slow-clotting blood and the red, almost semi-fluid, bone marrow, are sufficient to identify it, and confirmation is easily obtained by examination of a blood film, when the presence of basophil erythroblasts is diagnostic. Histological examination of the liver shows an engorgement of the sinusoids with primitive red cells, a condition known as leukostasis.

Both myeloid and erythroleucosis, but not, as far as is known, myelocytoma, are associated with a virus, enabling transmission by cell-free inocula to susceptible young chickens. There is evidence that mixed forms occur, giving the so-called erythro-myeloblastic leucosis. According to Darcel and Negroni (1954) Olson's tumour RPL/12, designated visceral lymphomatosis, is really an aberrant form of erythroleucosis. There has also been confusion regarding the viral status of the RPL/12 tumour, some workers failing to demonstrate a filterable agent. A compromise solution, and not a very satisfactory one, has been put forward by the report of the "Conference on Histopathology of Experimental Avian Lymphomatosis" (1959) where it was agreed by a majority that the intravascular form was an erythroblastosis, while the visceral form was associated with a very immature cell which was considered to belong to the lymphocytic series.

Recent studies of lymphoid, myeloid and erythroleucosis by Mommaerts, Beard and Beard (1953), Beaudreau and Becker (1958) and Becker, Beaudreau and Beard (1959), show certain constant differences in their enzymic activities and therefore in their metabolism. How much these differences depend on the virus infecting the cell, or on the cell type stimulated to neoplasia by the virus, is for future workers to ascertain.

Fowl paralysis and related conditions

The classic and common form of fowl paralysis is accompanied by clinical signs which are practically diagnostic. These are spastic paralysis of the legs and wings, and, less frequently, symptoms indicating that the cranial or intestinal nerves are affected (Siller, 1960*a*). The perching reflex is lost, and the bird often lies on its side in a characteristic attitude with one leg stretched forward and the other extended behind. The disease is not rapidly fatal, and birds can survive over prolonged periods if nursed. Occasionally affected birds may show distortion, depigmentation and paralysis of the iris, although this seems to be rarer than formerly, and is probably not in itself of much diagnostic value.

Examination of the peripheral nerves such as the vagi, brachials and sciatics usually shows them to be oedematous, thickened and exhibiting loss of striation. Actual tumour-like swellings may appear on the dorsal ganglia of the nerves or, less commonly, along their length. These lesions may be bilaterally symmetrical, involving nearly every peripheral nerve, or apparently confined to one or two nerves and not necessarily equally distributed.

Pullets with fowl paralysis may show visceral lesions. These usually affect the immature ovary, which resembles a mammalian salivary gland, being pink or cream-coloured and showing a distinctly lobulated structure. It is enlarged, but usually not grossly so. The mesentery may be thickened and have a whitish, granular appearance. Other viscera may show similar tumour-like lesions, but the ovary seems to be particularly prone to damage. The liver, spleen and bone marrow are usually macroscopically normal.

Histological examination shows a varying degree of infiltration of mononuclear cells into the oedematous nerves. The impression is that the oedema comes first, followed by a demonstrable demyelination and fatty change, and that cellular infiltration is a later event. Electron microscope studies (Deutsch & Siller, 1961) show a marked endoneural fibrosis, which is not very evident when the light microscope is used. The mononuclear cells are mainly mature lymphocytes and plasma cells, but occasional large cells resembling histiocytes, and even granulocytes, may be seen. There may be a peculiar beading along the myelin sheath, probably oedematous in origin, which is traversed by an apparently intact axon. Affected spinal ganglia usually show a reactive hyperplasia of the Schwann cells. Central lesions taking the form of perivascular cuffing with lymphoid cells may be found in the brain stem.

Early visceral lesions, e.g. in the liver or spleen, appear to start as a localized necrosis, which area is rapidly infiltrated by lymphocytes etc. to form small, well-vascularized nodules. The ovarian lesion probably arises primarily in the

adjacent coeliac ganglion and spreads to the ovary. It, too, is composed of a mixture of mononuclear cells, histiocytes, fibroblasts and occasional granulocytes. These visceral lesions, although grossly tumorous in nature, do not have the histological characteristics of a neoplasm and do not metastasize. They are more accurately designated lympho-granulomas, and are inflammatory in origin. Blood films and marrow smears show no abnormality (Campbell, 1956).

Rarely, a visceral or neural lesion may develop a true malignant character and invade locally or metastasize. Histological examination shows such lesions to be neoplastic and composed of a uniform population of immature lymphoid cells (lymphoblasts). The condition is then a lymphosarcoma or lymphoblastoma and it is indistinguishable from lymphoid leucosis. It is not surprising that such transformations occasionally occur, since malignant change in a chronically inflamed tissue is a well-known though happily not invariably phenomenon.

Ocular lymphomatosis

The ocular form of fowl paralysis is associated with a mixed infiltration of lymphocytes, plasma cells and granulocytes into the iris and ciliary body, causing a greyish, deformed and paralysed iris. Since iritis can and frequently does occur without the other stigmata of fowl paralysis, it can only be reasonably designated the "ocular form" when other typical lesions are present. The impression is that it is much more rare than formerly.

Osteopetrosis

The last condition that will be dealt with here is *Osteopetrosis gallinarum* (Jungherr and Landauer, 1938). This osteopathy has been frequently mentioned as developing in fowl paralysis (Jungherr and Landauer, 1938) or in experimental dirds after inoculation with lymphoid leucosis material (Burmester and Cottral, 1947) or myeloblastosis (Gross *et al.*, 1959). Jungherr (1952) refers to the condition as "osteopetrotic lymphomatosis". However, Brandly, Nelson and Cottral (1941) and Burmester and Cottral (1947) held that lymphomatosis and osteopetrosis were probably unrelated.

Holmes (1958, 1959) recently succeeded in transmitting a field case of osteopetrosis and demonstrated a causative virus for the first time. Through his kind co-operation this condition is now also being studied at the Cancer Unit at the Poultry Research Centre, Edinburgh.

Initial inoculation of day-old chicks with blood from a florid case results in well-developed bone lesions in 12-14 weeks, especially in males. The main bones involved are the long bones of the wing and legs, the digits developing lesions much later. The pectoral girdle may also be affected. The distribution of skeletal lesions in the fowl appears mainly to parallel the citrate content of the bones. Taylor, Moore & Hertelendy (1960) showed two categories of bones, one with high, the other with low citrate values. Osteopetrosis, in the earlier stages at least, affects only those bones with a low citrate content (Bell & Campbell, 1961). The swollen fusiform bones show a thickened periosteum and are highly vascular. The initial lesion as seen by X-rays seems to be an

endosteal proliferation of bone, followed by a progressive laminar deposition of periosteal bone. The medullary cavity is eventually obliterated by new bone with an abnormal architecture, due to enormously enlarged and elongated Haversian canals extending centripetally towards the shaft centre. These vascular spaces contain no marrow, but have a scanty fibro-cellular tissue. Anaemia results from the obliteration of the marrow. This stimulates an extramedullary myelopoiesis in the liver and kidneys which may be quite striking. The blood shows no change in the total red cell count, but many normoblasts showing variable basophilia are present, although there is a deficiency of white cells characteristic of a myelophthisic anaemia.

Some proerythroblasts occur in the peripheral blood, but not in sufficient numbers to resemble erythroleucosis (Bell & Campbell, 1961).

CONCLUSIONS

This brief survey of the conditions which have been regarded at some time or other as belonging to a complex of diseases designated the leucoses of the fowl enables us to form an opinion as to the validity of their inclusion in such a complex.

If the definition of leucosis as a neoplastic disease involving the precursors of lymphoid, myeloid and erythroid cells is accepted, then fowl paralysis in its various forms must be excluded, since although the primary inflammatory lesions may occasionally terminate in neoplasia, they *are* primarily inflammatory and thus differ profoundly from the three leucotic diseases, which are neoplastic from the outset. There is growing agreement that the so-called fowl paralysis tumours are reactive lymphogranulomas probably formed as a response to an initial acute inflammation of as yet unproven origin. Similarly, the oedema, myelin degeneration with the liberation of fat, infiltration with mononuclear cells of different types and the endoneural fibrosis of affected nerves are all features characteristic of inflammation rather than neoplasia. The work of Siller (1960*b*) on experimental allergic encephalomyelitis in the fowl, a condition which closely resembles neurolymphomatosis, may eventually help to throw light on the aetiology of fowl paralysis. The specificity of ocular lymphomatosis is in some doubt, since it seems identical to other iritises in which there is no reason to believe fowl paralysis is implicated. This is not to say that the condition does not exist as an entity, but it is certainly now much less common than formerly. The available evidence that fowl paralysis may occur in birds inoculated with any of the accepted leucosis agents, or even with intact living cells, is quite unsatisfactory and is capable of explanation in terms of the unmasking of latent infection or of infection with more than one virus. Conversely, fowl paralysis in any of its forms is very difficult to transmit experimentally, although Durant and McDougle (1945) claimed success, and there is little good evidence that any of the accepted leucoses developed in such inoculated birds. Again, in the wealth of literature dealing with the transmissible leucoses, no firm evidence is to be found of the induction of fowl paralysis in any form. In the terminology it is evident that much confusion has resulted from the use of the term "visceral lymphomatosis",

which some workers understand to be a genuine lymphoid leucosis, whilst others use it to designate the visceral lesions associated with fowl paralysis. Cole and Hutt (1951) concluded, in opposition to other workers such as Waters and Prickett (1944), Waters (1944), and Cottral, Burmester and Waters (1954), that leucosis is not egg-transmitted. They came to this conclusion as a result of their experiments with "visceral lymphomatosis", which in their case seems almost certainly to consist of the lymphogranulomatous lesions associated with fowl paralysis. However, Gordon, Coles and Stacey (1955) obtained some evidence that neurolymphomatosis may be egg-transmitted, an observation which seems to bring the conditions into line with the leucoses proper, where egg transmission is found to play a part. The evidence for the removal of fowl paralysis from the complex is summarized in papers by the author (Campbell, 1945, 1954 and 1956).

It is obvious that the term "visceral lymphomatosis" contributes largely to the confusion. It is proposed that the term be discarded and "lymphoid leucosis", as distinct from fowl paralysis granuloma (which can be neural, visceral or ocular), be substituted.

With regard to osteopetrosis the position is not so clear. It is not a neoplastic condition, but rather an osteopathy characterized by hyperplasia. It is, however, associated with a virus, and numerous reports show that it has occurred in greater or lesser degree in experimental birds used for transmission experiments with lymphoid or myeloid leucosis. In our experiments this has not happened and spontaneous osteopetrosis is unknown in our flock, although an occasional spontaneous case of leucosis does occur. Similarly, none of our experimentally induced osteopetrosis cases have developed any leucotic disease. Thus we cannot confirm as yet that the leucoses and osteopetrosis have a common aetiology.

A final word must be said about the recent proof by Carr (1956) that the virus of erythroleucosis can, under certain rather strictly defined circumstances, produce primary renal tumours of an adenomatous nature. The same virus can also, under certain conditions of dosage and site of inoculation, produce fibro-sarcomas (Oberling & Guerin, 1933). Carr has since obtained preliminary evidence that the osteopetrosis virus may produce similar but not identical renal tumours (personal communication). Foulds (1954) observed peculiar renal tumours in birds infected with the unique MH2 (Mill Hill) endothelioma, also a virus-associated tumour, but he did not consider that they originated in the kidney. If the debatable MH2 is set aside until more evidence is available, it does seem clear that a number of these viruses have multicellular oncogenic properties, and in this respect they may resemble the recently isolated polyoma virus (Steward, Eddy & Borgese, 1958).

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A DISCUSSION ON THE CLASSIFICATION OF THE AVIAN LEUCOSIS COMPLEX AND FOWL PARALYSIS

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The development of the term "avian leucosis complex" together with the history of the confusion in terminology of this group of diseases has already been discussed by Campbell (1961). For this reason the following discussion will be confined to a consideration of the classification of this group of diseases in relation to the facts and needs of the present day.

The need for a universally acceptable classification requires no stressing. Apart from the obvious advantage of a uniform terminology, a well-defined classification based on sound principles would facilitate the interpretation of data from various laboratories and enable these data to be applied more accurately and advantageously in the field.

In a paper such as this it is imperative that terminology be defined at the outset, and that suggested by Campbell (1961) will be used for the purposes of this discussion. The central feature of this classification is the separation of fowl paralysis granuloma in all its forms from the "avian leucosis complex". This involves a distinction between the visceral and the more common neural form of fowl paralysis granuloma, and lymphoid leucosis. Therefore, the main problem to be considered is whether there is good evidence for this separation and whether such a classification will assist in the understanding and future advancement of knowledge of this whole group of diseases. Consideration must therefore be given to the grounds on which such a separation could be made. These could be based on evidence derived from pathological studies, aetiological studies and/or observations in the field.

PATHOLOGY

The separation of fowl paralysis granuloma from the leucoses has been suggested by Campbell (1961) largely on the basis of the different histological pathogenesis. Early lesions in the nerves at times show evidence of some oedema and a variable degree of proliferation of Schwann cells with nuclear swelling. At this stage there is usually a light scattering of mononuclear cells, which appear to be derived from small perivascular foci. These cells include small, medium and large lymphocytes, "blast" cells and plasma cells. The latter cells are most evident in the early lesions and may be present in small groups adjacent to small blood vessels as well as scattered throughout the nerves. The perivascular foci of lymphocytes, which rarely contain plasma cells, enlarge (Figs. 1 and 2). At the same time the diffuse scattering of cells increases and the cells appear to spread out from these foci and eventually involve a large

part of the nerve. Plasma cells are now relatively less common; lymphocytes, including a variable proportion of immature lymphocytes, form the majority of the infiltrating cells. The density of infiltrating cells becomes greater until the nerve is a solid mass of lymphoid cells with no, or extremely few, plasma cells present (Figs. 3 and 4). Mitotic figures may be plentiful at this stage (Fig. 4) and evidence may be seen of infiltration outside the boundaries of the nerve (Figs. 3, 4 and 5).

The early lesions are indicative of damage to nerve tissue and a primary inflammatory change, but the later and more advanced changes are histologically indistinguishable from neoplastic disease. These latter lesions are by no means a rarity but are frequently encountered in birds that have died from fowl paralysis granuloma.

The visceral lesions seen associated with the neural form of fowl paralysis granuloma present an even greater pathological problem. In the author's experience lesions in the liver rarely start as foci of necrosis followed by granuloma formation, but more commonly as an increase in size and number of the lymphoid foci normally present in the liver. In some cases there is an increase in the more immature lymphoid cells and frequently in the myelocytes associated with these foci.

The author is in full agreement with Campbell (1961) that the most common proliferative visceral lesions occur focused in and around the ovary. However, these lesions are usually similar to the more advanced changes seen in nerves; plasma cells are usually scanty or absent and certainly are not present in greater numbers than can be seen associated with neoplastic lymphoid tissue; lymphoid cells of all degrees of differentiation may be present, the relative number of each cell type varying from case to case; mitotic figures can be plentiful; the lesions may appear infiltrative, frequently spreading through the mesentery and at times to adjacent organs such as the lungs and kidneys. In these latter two respects the visceral lesions have neoplastic characteristics. However, it must be pointed out that the pathological classification of this type of lesion is problematical. To quote Marshall (1956): "the distinction between neoplasia or inflammatory hyperplasia in the reticular tissues is of the utmost difficulty on histological grounds, as in both processes the reacting cells are derived from the same tissue." In birds this problem is made more difficult by the replacement of lymph nodes by a widespread distribution of lymphoid tissue (Biggs, 1956, 1957).

It has already been pointed out that the early neural lesions are indicative of a primary inflammatory change, but the frequent change to proliferative lymphoid lesions histologically similar to those of some types of lymphoid leucosis complicates the interpretation of these changes on histological grounds. Therefore, it is concluded that at present many of the lesions of fowl paralysis granuloma are indistinguishable from lymphoid leucosis on histopathological grounds alone, and that the more advanced lesions of fowl paralysis granuloma bear a close relationship to lymphoid leucosis. However, there are other considerations. Campbell (1961) has mentioned that the distribution of visceral lesions in fowl paralysis granuloma differs from lymphoid leucosis.

Also it must not be forgotten that in most cases of fowl paralysis granuloma the peripheral nerves are affected, and that a primary neoplastic disease of lymphoid tissue involving peripheral nerves so frequently is unprecedented.

AETIOLOGY

There is at present no substantiated evidence that fowl paralysis granuloma and the leucoses have separate aetiologies. Nevertheless, Blakemore (1939) induced fowl paralysis granuloma in chickens inoculated with preparations of tissues from field cases of this disease. He found that only 8 per cent of the induced cases of fowl paralysis granuloma had lymphoid tumours but, unfortunately, these were not described in detail. Burmester and Gentry (1954, 1956) and Burmester, Fontes, Waters, Bryan & Groupé (1960) have shown that RPL 12 virus will induce erythroblastosis and "visceral lymphomatosis" (lymphoid leucosis) with no significant incidence of neurolymphomatosis (neural form of fowl paralysis granuloma). However, Campbell (1961) has already pointed out that most of the reports of transmission experiments have led to conflicting results and furthermore, to results which can be interpreted in several ways. In the interpretation of results of transmission experiments consideration must of course be given to the possible unmasking of latent infection or infection with more than one virus. However, consideration must also be given to the fact that diagnosis of visceral lesions depends largely on gross and microscopic pathology. This difficulty presents a further problem in the interpretation of experimental results.

To illustrate some of these problems the results of two transmission experiments are briefly presented. These are two of several experiments made by Biggs and Payne (unpublished) in an attempt to establish a strain of transplantable lymphoid leucosis. Inoculi were, for this reason, suspensions of viable cells prepared from tumours taken from recently killed birds showing macroscopic lesions indicative of lymphoid leucosis.

Results

The result of these experiments are summarized in Table I.

Experiment 1. In the first experiment (BP1), cell suspensions were made from the tumorous liver and ovary of an 18-month-old Rhode Island Red × Light Sussex hen. Post-mortem examination showed that the liver was diffusely enlarged and there was diffuse tumour formation on the peritoneum and ovary which had spread to the left lung. The sciatic and brachial nerves were normal, a finding confirmed by histological examination. Histological examination of tissues from the ovary, peritoneum and lung showed a diffuse involvement with lymphoid cells. Tumour cells were seen to be scattered both intravascularly and extravascularly throughout the liver with denser accumulations around the veins and portal tracts. The majority of cells were undifferentiated lymphoid cells; mitoses were numerous.

Six 21-day-old chicks and nine six-day-old chicks were inoculated intramuscularly. Ten of the 15 inoculated chicks showed evidence of fowl paralysis granuloma within the experimental period of 117 days. The ages at which

TABLE I
THE RESULTS OF TRANSMISSION EXPERIMENTS USING WHOLE-CELL PREPARATIONS

Experiment	*No. of birds and age inoculated*	*Fowl paralysis*			*Fowl paralysis + Visceral lesions*			*Lymphoid leucosis*			*Total affected*		*Experimental period—days*
		No.	%	*Age in days*	*No.*	%	*Age in days*	*No.*	%	*Age in days*	*No.*	%	
BP 1	15 6 & 21 days old	8	53	50, 62, 97, 97, 97, 123, 132, 138	2	13	28, 43	—	—	—	10	66·6	117
BP 3	12 1 day old	4	33	38, 75, 151, 151	2	17	42, 42	—	—	—	6	50	151
BP 3/531	6 1 day old	—	—	—	—	—	—	2	33	17, 22	2	33	513
BP 3/531/586	7 14-day-old embryos	3	43	53, 58, 373	—	—	—	—	—	—	3	43	493

these birds died or were killed are shown in Table I. The two chicks which succumbed first also showed visceral lesions in the ovary and one had a small tumour at the site of inoculation. The point of interest in this experiment is that in one chick the transplanted cells were proliferating at the site of inoculation and these were similar to the cells seen in the ovary and sciatic nerve (Figs. 6, 7, 8). Whatever the status of the donor, cellular preparations induced a high incidence of fowl paralysis granuloma and these same cells were also apparently capable of proliferation in a homologous host.

Experiment 2. The second experiment (BP3) was similar in many respects but of more interest because it extended to three passages. The donor bird was a hen in poor condition which at post-mortem showed a moderately enlarged pinkish-grey liver with numerous pinhead-sized white foci throughout its substance. The spleen, kidney and ovary were diffusely enlarged. The sciatic and brachial nerves were macroscopically and microscopically normal. Histological examination showed that the spleen, kidney and ovary were diffusely infiltrated with lymphoid cells. The liver showed discrete foci of lymphoid cells in the parenchyma and around blood vessels. Scattered and small groups of lymphoid cells were present throughout the parenchyma, some apparently lying within sinusoids. The majority of cells were medium lymphocytes though all stages of differentiation were present. Mitotic figures were numerous. Examination of other birds from the same flock demonstrated that both fowl paralysis granuloma and lymphoid leucosis were present.

Preparations of the liver were used to inoculate 12 one-day-old chicks, cell suspensions were inoculated intraperitoneally in four and intramuscularly in four, and a portion of liver was implanted subcutaneously in four. Six of the 12 birds showed evidence of fowl paralysis granuloma within the experimental period of 151 days and these died or were killed at the ages shown in Table I. Two of these birds showed visceral lesions, one inflammatory lesions in the liver and the other an ovarian lymphoid "tumour". A cell suspension was prepared from the ovary and six one-day-old chicks were inoculated intraperitoneally. Two of these chicks showed lymphoid leucosis 17 and 22 days after inoculation, the other four showed no evidence of fowl paralysis granuloma or lymphoid leucosis during the experimental period of 513 days (Table I). In one chick there was a large white lymphoid tumour at the site of the ovary, with diffuse involvement of the peritoneum, kidneys and part of the liver. The second chick showed tumour tissue at the site of inoculation, throughout the peritoneum and infiltrating the proventriculus and intestinal wall, diffusely infiltrating the right lung, left testes and heart, and a diffuse and nodular infiltration of tumour cells in the liver. A cell suspension was prepared from the tumorous tissue of the liver of this chick. Seven 14-day-old chicks embryos were inoculated intravenously. In an experimental period of 493 days three cases of fowl paralysis granuloma occurred and in none of these were visceral lesions present (Table I).

The status of the original donor in this experiment again presents a problem, especially as it was known that both fowl paralysis granuloma and lymphoid leucosis were present in the flock. However, the significant points of this

experiment are: (1) cells from the original donor bird apparently induced fowl paralysis granuloma; (2) cells prepared from an ovarian "tumour" of one of these cases of fowl paralysis granuloma induced lymphoid leucosis only, which, in view of the short latent period, was most likely to have been the result of a direct cell transplant; (3) when cells from one of these cases of lymphoid leucosis were passaged, only fowl paralysis granuloma occurred in the recipients.

Whether it is considered advantageous or not to separate fowl paralysis granuloma from lymphoid leucosis, these results demonstrate that they are apparently in some way closely interrelated.

FIELD OBSERVATIONS

A similar relationship is found in the field, where it is not infrequent to find both fowl paralysis granuloma and lymphoid leucosis present in the same flock. Nevertheless, it is perhaps the observations made on field material that give the strongest support for the separation of these two conditions. Fowl paralysis granuloma tends to affect younger birds than does lymphoid leucosis. Recently in Great Britain fowl paralysis granuloma has become a problem in the broiler industry. Rarely, it may affect chicks four weeks of age, it is not uncommon in chicks six to eight weeks of age, and it is frequently seen in birds about four months old (Gordon, 1960). Visceral lesions, particularly involving the ovary, are seen in the younger birds as well as birds of the older age groups. Lymphoid leucosis on the other hand is only rarely seen in such young birds, and it most commonly occurs in birds six to nine months old.

CLASSIFICATION AND TERMINOLOGY

The most cogent evidence supporting a distinction between fowl paralysis granuloma and lymphoid leucosis is therefore the difference in: (1) age group affected, (2) distribution of organs and tissues affected, and (3) histopathogenesis. Whether such a separation assists in the understanding and future advancement of knowledge of these diseases has been made clear today, since a discussion such as this could not have taken place without such a distinction in terms. It is believed that these are good reasons to support the distinction in terms suggested by Campbell (1961). However, the evidence which has been presented today suggests that at present the exclusion of fowl paralysis granuloma from a group of diseases which includes one at least with which it appears in some way interrelated is unwarranted. Therefore, it is suggested that the group of diseases previously termed the avian leucosis complex remain as one group, and because the evidence supports the view that fowl paralysis granuloma is a separate disease entity with an inflammatory origin this group should be renamed the "avian reticuloses".

If a classification and terminology based wholly on pathology is correctly interpreted it can be accurately implemented, but it has serious limitations. The classification and terminology proposed by Jungherr, Durant and Lee (1941) and adopted in the United States of America is a good example. Lymphomatosis in this classification is applied to all proliferative lymphoid

lesions, neural, ocular and visceral, whether or not they are associated with neural lesions. This term, therefore, embraced the disease which Campbell (1961) has referred to as lymphoid leucosis. This has resulted in considerable confusion and has implied, though not intentionally, a unity of aetiology which at present is unfounded. The question of whether the lesions of fowl paralysis granuloma frequently result in neoplastic disease is immaterial to the present discussion but, because such lesions are often indistinguishable from those of lymphoid leucosis, a wholly pathological classification would be unsatisfactory. In agreement with Campbell (1961) it is considered that the term lymphomatosis should be discarded but, owing to the pathological similarity between many of the visceral lesions of fowl paralysis granuloma and lymphoid leucosis, it is considered that the use of the term granuloma could also lead to misunderstandings. Fowl paralysis is also an unsatisfactory term because it describes a symptom not always present. Therefore, it is suggested that this complex be termed Marek's disease, a term which has some

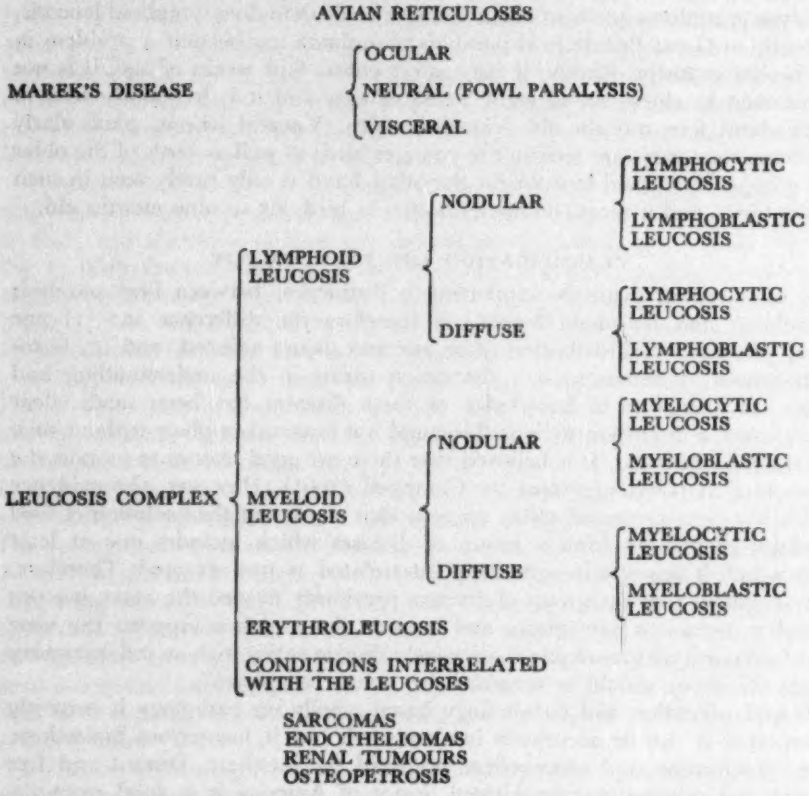

Fig. 9. Proposed classification of the avian leucosis complex and fowl paralysis.

precedence and which implies a disease and not a pathological entity. At present Marek's disease would include three forms; neural (fowl paralysis), visceral and ocular (Fig. 9). The latter is included because at present there is no evidence to support its separation on aetiological grounds. Thus the "avian reticuloses" would be divided into two major groups, Marek's disease and the leucosis complex.

Recently evidence has been forthcoming which indicates that there are aetiological relationships between the different leucoses as well as other virus-induced tumours of the domestic chicken. RPL 12 virus induces erythroblastosis, osteopetrosis and visceral lymphomatosis (lymphoid leucosis) (Gross, Burmester & Walter, 1959) and more recently Burmester (1960, personal communication) has induced similar lesions with cell-free preparations of lymphoid leucosis tissue taken from birds obtained from six separate poultry farms. This strongly supports the view that the RPL 12 virus is representative of the virus or viruses responsible for lymphoid leucosis. It has also been shown that two strains of leucosis, erythroblastosis strain R and myeloblastosis strain A, in low doses induce lymphoid leucosis (Burmester, Walter, Gross & Fontes, 1959) and that strain A also induces osteopetrosis and renal adenocarcinomas. More recently Burmester and Walter (1961) have induced lymphoid leucosis with low doses of the Rous sarcoma virus. Oberling and Guerin (1933), Stubbs and Furth (1935) and others (see Darcel, 1957) have shown that strains of erythroblastosis can induce sarcomata and in some cases endotheliomata, and Carr (1956) has induced renal tumours with a strain of erythroleucosis. It appears that a number of viruses may be responsible for lymphoid leucosis and that many have multipotential oncogenic properties. The foregoing evidence would suggest that all these forms of tumour should be included in the leucosis complex, bearing in mind that each strain may eventually prove to contain more than one virus.

The classification illustrated in Fig. 9 is suggested. The classification and terminology of the leucoses is similar to the classification put forward by Campbell (1961) with two exceptions: firstly, the addition of the group of conditions interrelated with the leucoses, and secondly, the division of nodular and diffuse lymphoid and myeloid leucoses into lymphoblastic and lymphocytic leucosis, and myeloblastic and myelocytic leucosis respectively. This suggestion has been made because in the author's experience a diffuse or nodular distribution is not necessarily related to the degree of differentiation of the neoplastic cell.

Even with a classification such as this one very real problem still remains. This is concerned with the diagnosis of visceral lesions, especially when neural lesions have not been observed. However, if the lesions of Marek's disease differ fundamentally from lymphoid leucosis then there is hope that in the future this may be demonstrated.

SUMMARY

Consideration is given to the grounds on which a separation of fowl paralysis from lymphoid leucosis can be made. These are discussed under the headings

of pathology, aetiology and field observations. It is concluded that the difference in (1) age group affected, (2) distribution of organs and tissues affected, and (3) histopathogenesis, warrants a distinction in terms for these two diseases. It is also considered that the exclusion of fowl paralysis in all its forms from a group of diseases which includes lymphoid leucosis, with which it appears in some way interrelated, is at present unwarranted. A classification and terminology is proposed.

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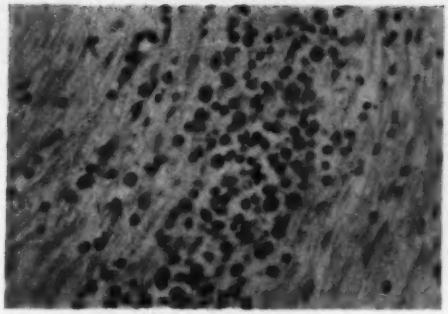

Fig. 1

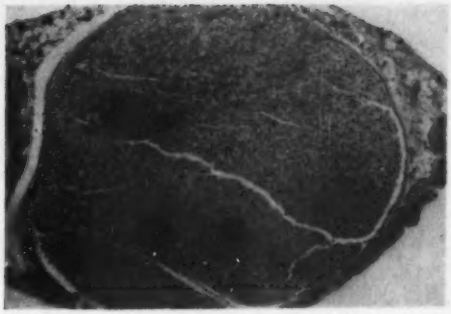

Fig. 2

Fig. 1. Early fowl paralysis. Longitudinal section of a sciatic nerve showing a small focus of lymphoid cells. The focus contains blast cells and all sizes of lymphocyte. Haematoxylin & eosin × 300.

Fig. 2. Fowl paralysis. Transverse section of one fasciculus from the coeliac plexus showing three perivascular foci and a light scattering of cells throughout the nerve. Haematoxylin & eosin × 50.

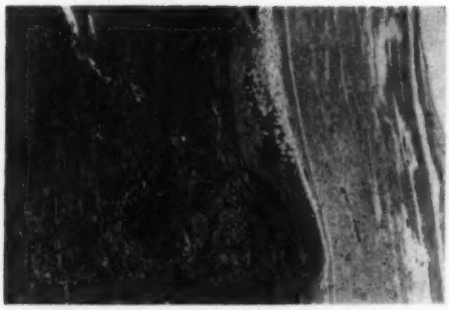

Fig. 3

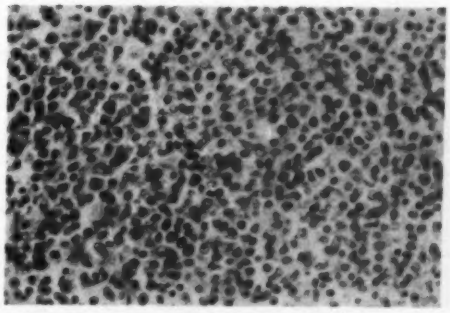

Fig. 4

Fig. 3. Fowl paralysis. Longitudinal section of a sciatic nerve showing dense and diffuse involvement of one fasciculus with lymphoid cells, and early involvement of the epineurium. Haematoxylin & eosin × 20.

Fig. 4. Fowl paralysis. High-power view of Fig. 3. Lymphocytes of all sizes are present, together with many mitotic figures. Haematoxylin & eosin × 300.

Fig. 5

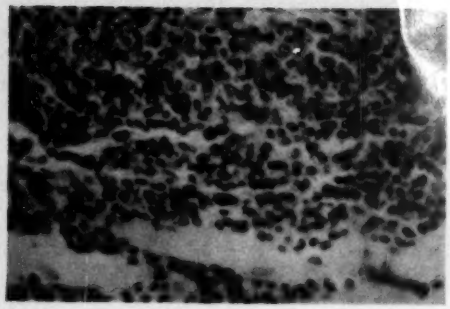

Fig. 6

Fig. 5. Fowl paralysis. Transverse section of one fasciculus from the coeliac plexus showing diffuse involvement of the fasciculus with spread to the surrounding mesentery. Haematoxylin & eosin × 20.

Fig. 6. Pectoral muscle of chick from Expt. BP1, 22 days after intramuscular inoculation with viable tumour cells, showing proliferation of transplanted cells at the site of inoculation and infiltration of the muscle (lower part of photograph). Haematoxylin & eosin × 300.

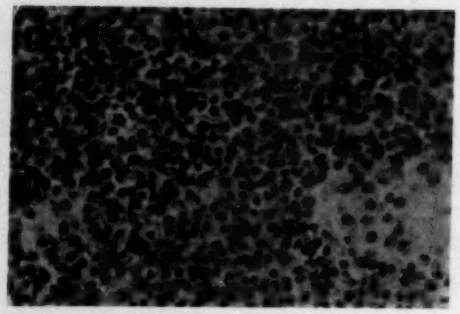

Fig. 7

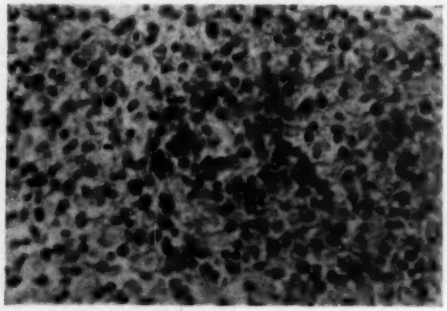

Fig. 8

Fig. 7. Ovary of the same chick as Fig. 6. Haematoxylin & eosin × 300.

Fig. 8. Sciatic nerve of the same chick as Fig. 6. Haematoxylin & eosin × 300.

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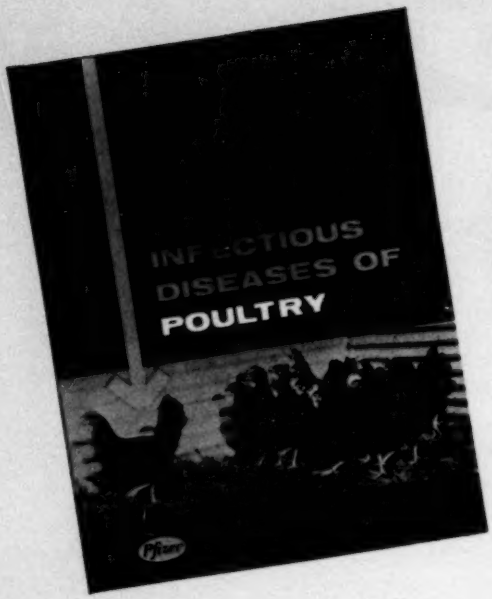

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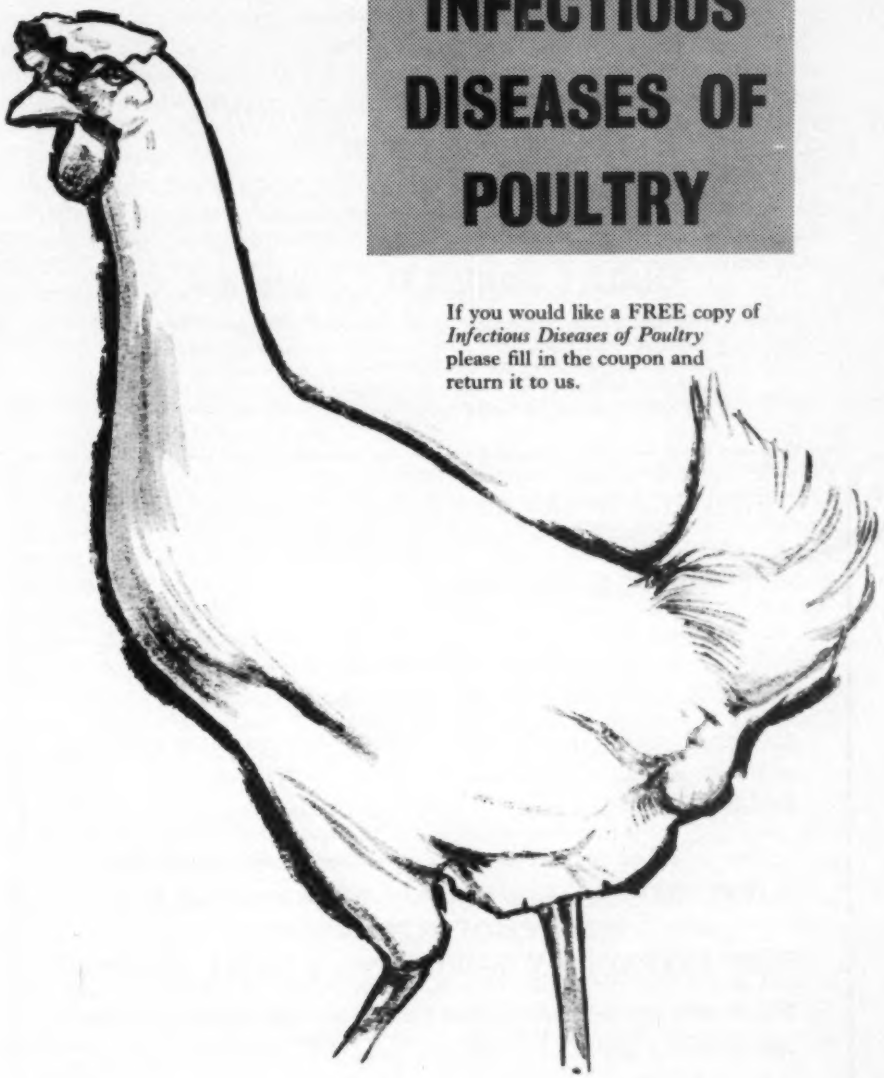

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B.V.J.

REVIEWS

Animal Health Yearbook, 1959. FOOD AND AGRICULTURE ORGANIZATION. H.M.S.O. 12s. 6d.

This annual, published under the auspices of the Food and Agriculture Organization, claims to contain "information on some 250 diseases in over 120 countries. In addition, there are well informed articles by world authorities on matters of current veterinary interest, with maps illustrating the present position in relation to certain epizootic diseases". There is no doubt that this publication does do all this and once one gets used to the codes it is relatively simple to establish the position regarding the various diseases and also their incidence. The tables show if the disease is widespread or if it is sporadic, or if it is unknown in that country.

The information has been compiled from replies to questionnaires.

It should prove invaluable to the officers responsible for State veterinary services in the various countries. I hope that in future years the Soviet Republics (U.S.S.R.) will figure in the publication; the present publication gives no information regarding the disease position in that vast country.

No State veterinary service should be without this publication.

H. G. LAMONT.

Radiography for the Veterinary Surgeon. R. N. SMITH. pp. 66, with 35 illustrations. Bristol: Wright. 13s. 6d.

This small volume includes eight chapters in which information is presented on the physical properties of X-rays; recording apparatus; the production and processing of film; dark-room construction and technique; and radiation hazards. The text is clear and concise and provides the sort of knowledge that would be of benefit to a practising veterinary surgeon when first setting up a radiographic unit. Several of the commercial companies that deal with radiographic equipment, however, are prepared to supply expert advice on these matters free of charge. Furthermore two firms have in recent years made a free course of instruction in radiography available annually to practitioners. In the presence of this sort of aid it is doubtful whether the present book will be used very frequently for reference since it will not in fact be fulfilling a need.

L. C. VAUGHAN.

Farm Animals in Health and Disease. W. R. WOOLDRIDGE. pp. xvi + 533. London: Crosby Lockwood. 2nd edn. 25s.

To have the claim on the dust cover that "This book provides a complete survey of all types of animal disease and the measures of prevention and control necessary to reduce it", is a handicap few volumes could overcome. That this one comes as close as it does is a tribute to the range and skill of its author. If it is viewed as a survey of the diseases occurring in farm animals in Great Britain, serious omissions are remarkably few. Dr. Wooldridge has

succeeded in bringing together in a systematic way a vast amount of scientific and practical information and in presenting it in a manner which should be easily understood by the lay readers for whom the book was written.

The first five chapters of a general nature are followed by individual chapters on the diseases of cattle, sheep, goats, pigs, horses, poultry and rabbits. Prevention is emphasized throughout. As in the first edition excellent photographs are a feature and seldom does the reader have to ask himself "Why did the author include this plate?" Most of them tell their story admirably although there are a few which could have been omitted without loss, e.g. plate 14b showing an advanced case of tuberculosis, plates 16a and 16b depicting calves with scours and husk, the rather pointless comparison between normal and aborted calves (plates 24a and b) and plate 36a showing an apparently normal pig as an example of weight loss due to virus pneumonia.

But these are details of small importance against the overall excellence of a book which should find ready acceptance among students of agricultural schools and the better class of livestock owners.

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THE BRITISH VETERINARY JOURNAL

The August issue (Vol. 117, Number 8) will contain the following papers:

J. H. Whitlock *Dept. of Pathology, Cornell University, New York.*	Parasitology, Biometry and Ecology.
J. Jansen *Institute of Infectious Diseases, Utrecht, Netherlands.*	Duck Plague.
B. L. Nestel *Research Dept. of the Sugar Manufacturers' Assoc., Jamaica.*	A note on the effects of Chlorpromazine injections at weaning on the subsequent live-weight gains of Beef Calves of both European and Zebu Breeding.
M. P. Johari and P. C. Gangwar *College of Veterinary Science & Animal Husbandry, Mathura, India.*	The Technique of Vasectomy (Vasoligation) in Cattle and Buffaloes.
H. E. Marthedal and Grethe Velling *Poultry Research Laboratory, Copenhagen.*	Haemorrhagic Syndrome in Poultry.
John Pasfield *Horsham.*	The Royal Dairy Show.

NOTICE TO CONTRIBUTORS

1. *The British Veterinary Journal* publishes original papers and reviews on all aspects of veterinary science and kindred subjects. Accounts of clinical observations are published and, in the form of letters to the editor, preliminary reports of scientific studies. Reviews should, in general, be written in support of original investigations.

2. *Manuscripts*, written in the English language, should be sent to the Editor, *The British Veterinary Journal*, 7 and 8 Henrietta Street, London, W.C.2. Papers are accepted for publication on the understanding that they have not been published and are not being considered for publication elsewhere, and that they may not be re-published without sanction from the publishers.

3. Contributions, which may be subject to editorial revision, should be condensed as far as possible and should be submitted as a top typewritten copy on one side of the paper only, with double spacing and ample margins. The spelling should be that of the Oxford English Dictionary.

4. Manuscripts should be headed with the title of the paper, the name and postal address of the author or authors, or, where applicable, the address of the institution where the work was done. They should conclude with a factual summary equal to about 3 per cent. of the length of the paper. References to previous work should be cited in the text with the author's name and the year of publication in parentheses, e.g., "Brown (1957) showed that . . ." Where there are more than two authors the names of all should be cited on the first occasion in the text and thereafter only the first followed by *et al.*, e.g., "Brown *et al.* (1957) . . ." In the list of references at the end of the paper all the authors' names and initials should be included. The references should be listed in alphabetical order of the surnames of the authors, and the titles of the journals should be abbreviated in accordance with the *World List of Scientific Periodicals*, e.g., Brown, A. B. (1957) *Brit. vet. J.*, **113**, 217.

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